Viral hepatitis: Which screening measures are recommended to exclude viral hepatitis before initiating a systemic treatment for psoriasis and how should patients who tested positive be managed with regard to their psoriasis?

Updated Version (changes to version 2021 are marked in blue)

A systematic review was conducted. The Method & Evidence Reports can be found below.

The update of this chapter was developed together with Prof. Pietro Lampertico, Milan, Italy and Prof. Vincent Mallet, Paris, France nominated by the European Association for the Study of the Liver (EASL). The EASL gave their final approval.

Results/Answer:

a. Screening

We **recommend against** screening for **hepatitis A, D or E** as routine measures before starting a systemic treatment.	↓↓	STRONG CONSENSUS 100 % Agreement EXPERT CONSENSUS DEVELOPED TOGETHER WITH THE EASL

Testing for hepatitis A, D, E shall be done only if indicated by anamnesis, elevated liver enzymes, clinical signs and symptoms but not as routine screening parameters.

We **recommend** screening patients for **hepatitis B** (HBsAg, anti-HBs, anti-HBcore) as a routine measure before starting a treatment with cyclosporine, deucravacitinib, methotrexate or biologics.	↑↑	STRONG CONSENSUS[1] 100 % Agreement EXPERT CONSENSUS DEVELOPED TOGETHER WITH THE EASL
We **recommend** following the algorithm presented in figure 1 for further testing and the interpretation of the **hepatitis B** test results.	↑↑	STRONG CONSENSUS 100 % Agreement EXPERT CONSENSUS DEVELOPED TOGETHER WITH THE EASL

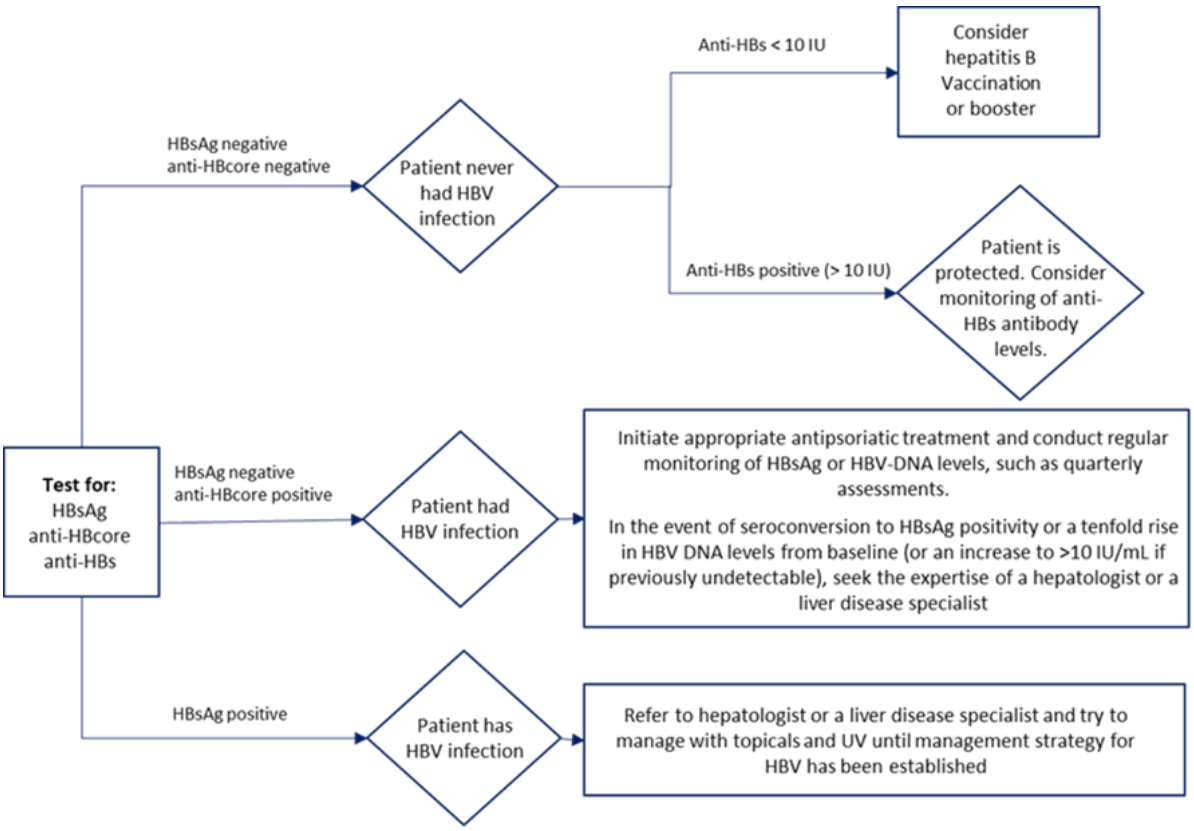
1 due to personal-financial conflict of interest 4 abstentions

We **recommend** screening patients for **hepatitis C** as a routine measure before starting a treatment with methotrexate, deucravacitinib or biologics.	↑↑	STRONG CONSENSUS[1] 100 % Agreement EXPERT CONSENSUS DEVELOPED TOGETHER WITH THE EASL
In case of positive findings for anti-HCV antibodies, **we recommend** testing for HCV RNA. In case of positive HCV RNA, we **recommend** referral to a hepatologist/ liver expert for treatment/management.	↑↑	STRONG CONSENSUS 100 % Agreement EXPERT CONSENSUS DEVELOPED TOGETHER WITH THE EASL

[1] due to personal-financial conflict of interest 4 abstentions

If anti HCV antibodies are positive and HCV RNA are negative after a recent anti-HCV treatment, communication with the treating hepatologist/ liver expert regarding liver fibrosis should be done. Positive anti-HCV antibodies and negative HCV RNA without a reported previous anti-HCV treatment indicate a resolved HCV infection and do not need a further referral to a hepatologist/liver expert.

Figure 1: Algorithm for the interpretation of the hepatitis B test results



List of abbreviations: Anti-Hbcore: Antibody to hepatitis B core antigen; Anti-HBs: Hepatitis B surface antibody; HBsAg: Hepatitis B surface antigen; HBV: Hepatitis B Virus

CONSENSUS: 94%

b. Choice of treatment

We **recommend** that treatment decision for psoriasis and HBV for patients with positive test result for HBsAg should always be taken together with a hepatologist/ liver expert.	↑↑	CONSENSUS 94%  EXPERT CONSENSUS DEVELOPED TOGETHER WITH THE EASL
Currently, there is insufficient evidence to give preference to one antipsoriatic treatment over another for HBsAg-negative/ anti-HBcore-positive or anti-HCV-positive and HCV RNA-negative patients. For these patients, we **suggest** selecting the treatment most suitable for the patient's psoriasis*, considering the very limited data available on the risk of HBV reactivation with newer drugs. * applies to the treatments discussed in this guideline	↑	STRONG CONSENSUS[1]  EVIDENCE AND CONSENSUS BASED, SEE METHODS & EVIDENCE REPORT DEVELOPED TOGETHER WITH THE EASL

[1] due to personal-financial conflict of interest 4 abstentions

The available data published is insufficient to give strong recommendations for or against using the available antipsoriatic drugs in patients with moderate-to-severe psoriasis, who are HBsAg positive.

As the choice and timing of treatment options for patients with psoriasis, who are HBsAg positive, can be complex, the group recommends an interdisciplinary collaboration with a hepatologist/ liver expert (see also Figure 1). They can provide guidance on the most appropriate therapy for hepatitis B, as well as the optimal timing for the initiation of systemic antipsoriatic therapy.

Table 4 in the methods report offers a summary of reported cases of reactivation. Reported cases need to be seen in correlation to approval date, especially with years and numbers of psoriasis patients with hepatitis exposed to the drug. This holds true in particular for deucravacitinib. For detailed information, see methods report.

For some of the treatments, hepatitis is mentioned as a contraindication in the SmPC, although clinical practice, available case series or registry data may indicate a safety profile in line with treatments where this is not mentioned as a contraindication. This hold particularly true for methotrexate, where study data indicates at least no increase in liver fibrosis [1].

c. Monitoring for reactivation during treatment

To monitor for the reactivation of viral hepatitis in patients who are HBsAg-negative/anti-HBcore positive, we **recommend** regular testing for HBsAg and/or HBV-DNA (e.g. every 3 months) during systemic treatment.	↑↑	STRONG CONSENSUS 100 % Agreement EXPERT CONSENSUS DEVELOPED TOGETHER WITH THE EASL
We **recommend** recording all treatment initiations and follow up visits of psoriasis patients with concomitant HBV or HCV cases in drug registries.	↑↑	STRONG CONSENSUS 100 % Agreement EXPERT CONSENSUS DEVELOPED TOGETHER WITH THE EASL

The Guideline Group evaluated the benefits and drawbacks of using HBsAg or HBV-DNA tests to monitor patients with past HBV infection for HBV reactivation (HBVr). While the HBV-DNA test is costlier, its increased sensitivity in early detection of HBV reactivation is notable, as HBV-DNA levels typically rise before HBsAg seroreversion and ALT level spikes. However, this evidence primarily pertains to hematological patients, particularly stem-cell transplant recipients, and not to patients with psoriasis. [2] Consequently, recommending one testing method over the other in the context of psoriatic patients is difficult without more specific evidence.

Living systematic review of the evidence on psoriasis treatment and viral hepatitis.

Table 1: History

Version	Search Date	Number of new studies	Additional information added	Implications for conclusions
Update 2	October 2022	5	See below	See below
Update 1	June 2021	6	See below	See below
Original	September 2019	22	n/a	n/a

Summary of methods and results (2023)

Authors: A. Pennitz, I. Vader (Update 2), M. Kinberger (Update 1), R. Jakubzyk (Original version)

Update 2 – December 2022 (blue = new study or additional data)

What was the aim of this systematic review?

The aim of this review update was to continuously inform the guideline development group of new evidence on patients with psoriasis vulgaris and coexisting viral hepatitis.
Many systemic psoriasis treatments modulate immune functions and can reactivate hepatitis, and are known to cause liver injury. However, patients with severe psoriasis and viral hepatitis still need systemic treatment. In this systematic review we investigated the safety and efficacy of systemic psoriasis treatment options for patients with concomitant viral hepatitis.

What did we do?

Two databases were searched systematically. We only included studies with patients treated with systemic psoriasis therapies who also had viral hepatitis B or C. We assigned Levels of Evidence for all studies included using the Center of Evidence Based Medicine Oxford recommendations [3] and RoB 2.0 tool [4] for the randomized trials. For details, see Methods Report.

What are the main results of the review?

We found 3 prospective studies [5-7], 2 register studies [1,8] and 28 retrospective studies [9-36] with 1758 patients with psoriasis vulgaris and coexisting viral hepatitis (hepatitis B n=1363; hepatitis C n=395).

Hepatitis B

- Prospective data
  - In a study by Chiu et al. 49 patients with psoriasis and hepatitis B were treated with secukinumab. A reactivation of hepatitis B was reported in 7 of 49 (14.3%) patients (risk of bias high) [6].
  - In a cohort study Ting et al. reported hepatitis B reactivation in 3 of 48 (6.3%) patients with isolated anti-HBc or resolved HBV infection treated with ustekinumab (Oxford Level of Evidence 3) [5].

- Al Mutairi and Abouzaid reported that of 32 patients treated with biologics (ADA, ETA, UST), none suffered from hepatitis reactivation, an increase in transaminases or viral load. A PASI75 response was reported in all 32 patients (risk of bias high) [7].

- Retrospective data
  - Acitretin
    - Chularojanamontri et al. reported that viral reactivation did not occur in 9 patients treated with acitretin [31].
  - CsA
    - Chularojanamontri et al. reported that viral reactivation did not occur in 2 patients treated with ciclosporin [31].
  - MTX
    - Tang et al. reported that 15 of 370 (4.1%) hepatitis B patients treated with MTX developed liver cirrhosis [1].
    - Chularojanamontri et al. reported that 2 of 6 (33.3%) patients treated with MTX suffered from viral reactivation [31].
  - TNFi
    - ADA: A total of 8 studies with 38 patients reported no hepatitis B reactivation in patients treated with adalimumab [11,13,17,19,22,25,34,35]. A total of 3 studies with 29 patients reported a PASI75 response in 28 (96.6%) patients treated with adalimumab.
    - ETA: A total of 8 studies with 43 patients reported hepatitis B reactivation in 3 (7.0%) patients treated with etanercept [11,13,17-19,23,25,31]. A total of 3 studies with 14 patients reported at least a PASI50 response in 13 (92.9%) patients treated with etanercept [13,18,25].
    - IFX: A total of 5 studies with 13 patients reported a hepatitis B reactivation in 1 (7.7%) patient treated with infliximab [13,17,18,31,35]. A total of 2 studies with 2 patients reported a PASI75 response in 1 (50%) patient treated with infliximab [13,18].
  - UST
    - A total of 7 studies with 111 patients reported a hepatitis B reactivation in 4 (3.6%) patients treated with ustekinumab [10,15,18,21,28,35,36]. One study reported a PASI75 response in 5 of 14 (35.7%) patients [10] and one study reported a PASI50 response in 1 of 1 (100%) patient [18].
  - SEC
    - A total of 5 studies with 60 patients reported a hepatitis B reactivation in 1 (1.7%) patient treated with secukinumab [24,29,30,33,35]. One study with 5 patients reported a "complete clearance" of psoriasis lesions in all 5 patients [33]. One study with 20 patients reported a PASI75 response in 100% (20/20) of patients, a PASI90 response in 90% (18/20) and a PASI100 response in 63% treated with secukinumab [30]. Qin et al. reported that 1 of 14 (10.9%) patients with resolved HBV infection treated with secukinumab developed hepatitis with negative HBV load [30].
  - More than one treatment
    - A total of 8 studies with 217 patients treated with more than one drug (conventional and biologics) reported a hepatitis B reactivation in 1 (0.5%) patient [8,9,16,20,25,27,31,35]. One study with 359 patients reported a total of 561 treatment episodes with more than one drug (only biologics). A total of 88/561 (15.7%) HBV reactivations were reported [26]. Gargiulo et al. reported a PASI100 response in 12/17 (70.59%) and a PASI90 response in 15/17 (88.24%) patients treated with more than

one treatment [27]. Chiu et al. reported a mean PASI improvement of 75.1% ± 21.6 in patients with chronic HBV infection, 76.2% ± 18.7 in patients with occult HBV infection and of 78.5% ± 18.5 in patients with resolved HBV infection [26].

Hepatitis C

- Prospective data
  - In a study by Chiu et al. 14 patients with psoriasis and hepatitis C were treated with secukinumab. A reactivation of hepatitis C was reported in 1 of 14 (7.1%) patients (risk of bias high) [6].
  - AlMutairi and Abouzaid reported that of 7 patients treated with TNFi (ADA, ETA), none sufferd from hepatitis reactivation, an increase in transaminases or viral load. A PASI75 response was reported in all 7 patients (risk of bias high) [7].
- Retrospective data
  - Acitretin
    - Chularojanamontri et al. reported "no worsening of HCV infection" during acitretin treatment in 1 patient with psoriasis vulgaris and hepatitis C [32].
  - CsA
    - Chularojanamontri et al. reported "no worsening of HCV infection" during ciclosporin treatment in 1 patient with psoriasis vulgaris and hepatitis C [32].
  - MTX
    - Tang et al. reported that 19 of 174 (10.9%) hepatitis C patients treated with MTX developed liver cirrhosis [1].
    - Chularojanamontri et al. reported "no worsening of HCV infection" during MTX treatment in 4 patients with psoriasis vulgaris and hepatitis C [32].
  - TNFi
    - ADA: A total of 3 studies with 27 patients reported no hepatitis C reactivation in patients treated with adalimumab [18,22,34]. In 20 of 27 (74.1%) patients, a PASI75 response was reported [18,22,34].
    - ETA: A total of 4 studies with 25 patients reported no hepatitis C reactivation in patients treated with etanercept [12,14,18,25]. A total of 3 studies with 20 patients reported a PASI75 response in 12 (60%) patients treated with etanercept [14,18,25].
  - UST
    - A total of 2 studies with 15 patients reported hepatitis C reactivation in 2 (13.3%) patients treated with ustekinumab [10,36].
  - SEC
    - A total of 2 studies with 33 patients reported 1 (3.0%) HCV reactivation in patients treated with secukinumab [24,29].
  - More than one treatment
    - A total of 6 studies with 33 patients reported zero cases of hepatitis C reactivation in patients treated with more than one systemic drug (conventional and biologics) [16,18,23,25,27,32]. One study with 61 patients reported a total of 112 treatment episodes with more than one drug (biologics). A total of 14/112 (12.5%) HCV reactivations were reported [26]. Gargiulo et al. reported a PASI100 response in 2/4 (50%) patients treated with more than one treatment [27]. Chiu et al. reported a mean PASI improvement of 75.2% ± 23.0 in patients treated with more than one treatment [26].

Key message

Hepatitis B reactivation was reported in 22 of 629 patients who received systemic psoriasis treatment. One study with 359 patients reported 561 treatment episodes with more than one drug and a total of 88/561 (15.7%) HBV reactivations.

Hepatitis C reactivation was reported in 4 of 130 patients who received systemic psoriasis treatment. One study with 61 patients reported 112 treatment episodes with more than one drug and a total of 14/112 (12.5%) HCV reactivations. Very few prospective studies and few retrospective studies are available. The reporting on whether patients have also received antiviral treatment during psoriasis therapy is inconsistent or incomplete. In addition, the antigen and antibody status of hepatitis B patients is reported inconsistently, hence further differentiation by status is not possible. Transaminases levels almost remained stable in the reported studies.

In 64 of 81 (79.0%) patients with psoriasis vulgaris and hepatitis B or C treated with TNFi a PASI75 response was reported in retrospective studies. Prospective data was only in one study available in which all patients (n=32) with psoriasis vulgaris and hepatitis B showed a PASI75 response after a treatment with ADA, ETA or UST (risk of bias high). However, a direct comparison with non-hepatitis patients is missing.

How up-to-date is this review?

We searched for studies that have been published up to 27 October 2022.

Methods

Update 2

Inclusion criteria

Apart from the newly included drug deucravacitinib we did not change the search strategy and the inclusion criteria of the previous version.

Table 2: Eligibility criteria for the review update on psoriasis and viral hepatitis

Patients	Inclusion: only adult patients with a clinical diagnosis of psoriasis and a concomitant hepatitis B or C being treated for psoriasis Exclusion: patients with psoriatic arthritis only
Intervention	Conventional systemic treatment (acitretin, apremilast, ciclosporin, fumarates, methotrexate) and biologicals (TNFi: adalimumab, etanercept, certolizumab pegol, infliximab; anti-IL12/23: ustekinumab; anti-IL17: bimekizumab, brodalumab, ixekizumab, secukinumab; anti-IL23: guselkumab, risankizumab, tildrakizumab; tyrosinkinase-2-inhibitor: deucravacitinib (new))
Comparator	Comparisons with another included drug and/or placebo
Outcomes	Change in skin lesions based on PASI (Psoriasis Area Severity Index) or PGA (Physician Global Assessment) or another study specific assessment. Transaminases, viral load or other study specific outcomes Type and proportion of other adverse events Quality of life based on SF-36 (The Short Form (36) Health Survey), DLQI (Dermatology Life Quality Index) or another study specific assessment.
Study Design	Inclusion: randomized controlled trials, clinical trials (with and without comparison group), cohort studies, case control studies, cross sectional studies and case series Exclusion: case reports

Information sources

The search strategy was updated and the databases MEDLINE Ovid from 1946 and Embase Ovid from 1974 were searched for the period June 2021 to 27 October 2022. The newly included drug

deucravacitinib was searched for the period January 2021 to 27 October 2022. The full search strategy is shown in the Appendix (Table 6 and Table 7) below. We screened all identified abstracts/titles for eligibility. Included titles/abstracts were then screened as full texts based on the above listed eligibility criteria (see Table 2).

Data collection, statistical analysis and evaluation

We performed the screening and did the data extraction using a standardized form. We recorded all full-texts excluded and the primary reason for exclusion (see below).

Methodological quality assessment/ Risk of bias assessment

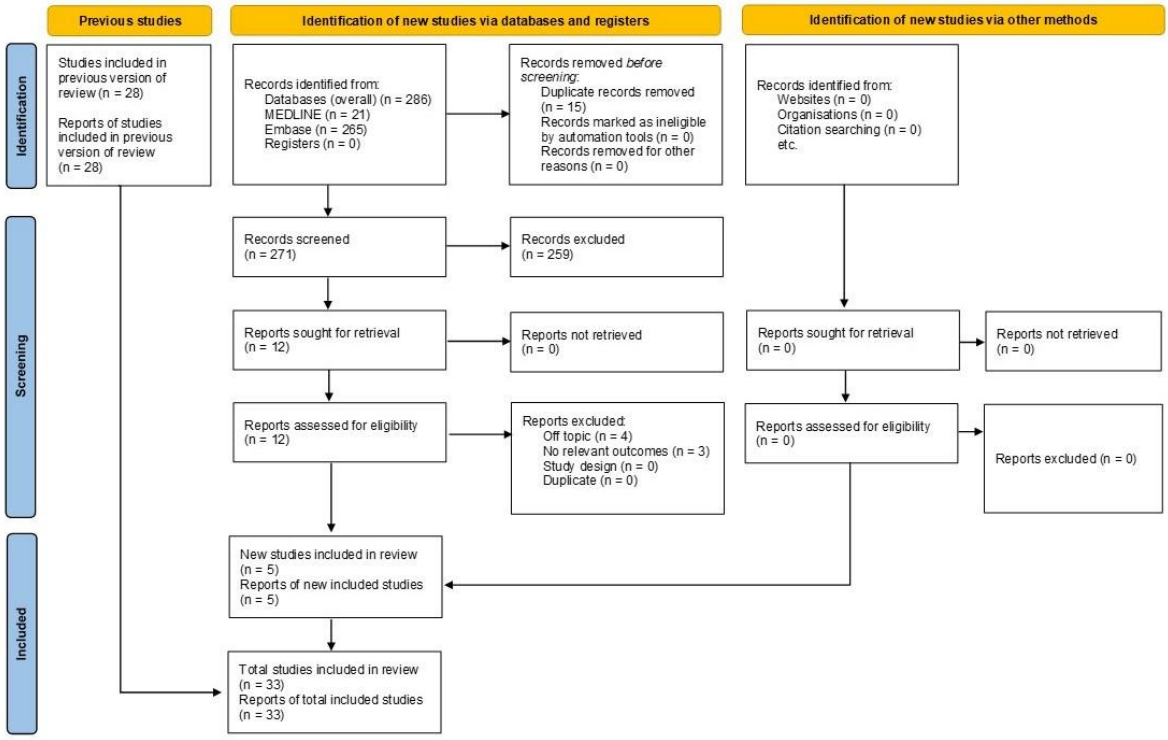
We assigned Levels of Evidence for all studies included using the Center of Evidence Based Medicine Oxford recommendations . To assess risk of bias in randomized trials we additionally used the RoB 2.0 tool [4].

Results

Our update search yielded 286 citations, 5 of which fulfilled the inclusion criteria [26-30] (see study selection flow chart, Figure 2).

No studies on systemic treatment with apremilast, bimekizumab, certolizumab pegol, fumarates, deucravacitinib and guselkumab were identified that reported outcomes for viral hepatitis neither in the original search nor in the update.

Figure 2: Study selection flowchart for the selection of studies for the review update 2 on psoriasis and viral hepatitis



Based on the 'Levels of Evidence - Center of Evidence Based Medicine Oxford recommendations' all retrospective studies were categorized level 3. Results of the additional assessment for prospective randomized studies with Risk of Bias Tool 2 (RoB 2) [4] are shown in Table 3. In the update, no further prospective randomized studies were found.

Table 3: Risk of bias in prospective studies (no new data since 2019)

Abbreviation:
⊕ = high risk of bias
? = unknown risk of bias
⊖ = low risk of bias

Author (Year)	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Al Mutairi, N. and Abouzaid, H.A. (2018)	⊕	⊕	⊕	⊖	⊖	⊕
Chiu H. Y. et al. (2018)I	⊕	⊕	⊕	⊖	⊖	⊕

RISK OF BIAS – PROSPECTIVE RANDOMIZED STUDIES

Data for overall 1758 patients with psoriasis and viral hepatitis was extracted. Of those, 1363 patients suffered from hepatitis B infection and 395 from hepatitis C infection. The tables (Table 4 and Table 5) below are providing detailed information, sorted by medication used.

Table 4: Hepatitis B

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
		Acitretin																	
Chularojanamontri, L. et al. (2020)[II]	Thailand	9	Acitretin	20.4 ±25.8	55.8±9.0	11.1	/	/	/	/	/	/	/	5/11	2/11 / = 1/11	none (4/11) LAM/TEN/EFA[2] (1/11) LAM/TEN[2] (1/11) TEN/LAM[2] (1/11) LAM[2] (1/11) LAM/ENT[2] (1/11)	0	/	3
		ADA																	
Piaserico, S et al. (2017)[II]	Italy	17	ADA	27*	50.8±12.5	35.3	/	21.2±6.9	16/17	39±25.4	40.4±25	39.7±27.8	44.9±30.4	0	0	LAM[1] (8/17) LAM/ENT[1] (1/17)	0	/	3
Fotiadou, C. et al. (2011)[II]	Greece	3	ADA	12±3	53.7± 10.6	33.3	6-24	14.1±2	3/3	19.3±2.1	20.7±1.2	21±2.6	21.3±2.5	0	0	none	0	/	3
Nosotti, L. et al. (2010)[II]	Italy	3	ADA	9.1±3.7	54±7.2	33.3	/	12.1±13.7	/	13±1.7	18.7±4.2	"unchanged"	"unchanged"	0	0	none	0	/	3
Navarro, R. et al. (2014)[II]	Spain	2	ADA	11 26	74 68	50	/	/		17 9	19 21	20 14	20 43	/		none	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
Snast, I. et al. (2017)[II]	Israel	2	ADA	12 72	55 69	0	63.7*	26.1 BSA 50	2/2 PASI50	35 19	29 34	34 24	42 14	0	0	none	0	Pneumonia (1/2)	3
Cho, Y.T. et al. (2012)[II]	Taiwan	1	ADA	27	44	0	14	/		15	46	22	34	0	0	none	0	none	3
Ozcelik, S. et al. (2020)[II]	Turkey	1	ADA	48	55	0	/	/	/	29	22	26	16	0	0	none	0	/	3
Narcisi, A. et al. (2020)[II]	Italy	9	ADA	20±5.2	59±9.4	44.4	/	18.44± 4.14	PASI100 7/9 PASI75 2/9	32.1±16.8	"no worsening"	23.6±19.4	"no worsening"	2/9	"no worsening"	TEN (2/9) LAM (2/9) none (5/9)	0	no SAE	3
		CsA																	
Chularojanamontri, L. et al. (2020)[II]	Thailand	2	CsA	21.5±10.6	43.5±2.1	0	/	/	/	/	/	/	/	2/2	/ = 1/2	LAM[2] (1/2) TEN[2] (1/2)	0	/	3
		ETA																	
Prignano, F. et al. (2011)[II]	Italy	11	ETA	8.6*	61.4*	27.3	7.3	/		"unchanged"				0	0	none	0	/	3
Snast, I. et al. (2017)[II]	Israel	8	ETA	55.2±46.3	57.3±12.2	37.5	63.7*	19.8±2.7 BSA 50 (4/8)	8/8 PASI50	27.6±16.8	22.2±7.2	24±9.2	19.5±8.5	0	0	LAM[2] (1/8)	0	none	3
Navarro, R. et al. (2014)[II]	Spain	7	ETA	28.7±20.7	60.6±15.4	28.6	/	/		34.9±14.9	34.7±21.4	44±23.4	32.6±19.6	/		none	0	/	3
Cho, Y.T. et al. (2012)[II]	Taiwan	6	ETA	24.8±12.7	42.6±4.1	16.7	31.3± 13	/		34.5±26.7	35.5±8.2	33.3±24.6	47±28.9	2	2	LAM[2] (1/6) LAM/ENT[2] (1/6)	3/6	none	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
Nosotti, L. et al. (2010)[II]	Italy	4	ETA	10.5±5.7	51.3±5.7	0	/	7.4±4.6	/	23.5±3.1	28.3±5.7	"unchanged"	"unchanged"	0	0	LAM[2] (1/4)	0	/	3
Fotiadou, C. et al. (2011)[II]	Greece	3	ETA	12.1±5.9	49.7±14	66.7	6-24	12.1±2.2	3/3	17.3±1.5	18.3±1.5	20.3±3.1	22.7±3.2	0	0	LAM[2] (1/3)	0	/	3
Navarro, R. et al. (2013)[II]	Spain	3	ETA	27±19	43.7±13	33.3	25*	19.7±4.8	2/3 PASI50	28.3±4	44.3±14.6	46.3±3	45.7±13.7	1	0	ADE/ENT[2] (1/3) LAM[2] (2/3)	0	none	3
Chularojanamontri, L. et al. (2020)[II]	Thailand	1	ETA	1	70	0	/	/	/	/	/	/	/	/	/	none	0	/	3
IFX																			
Navarro, R. et al. (2014)[II]	Spain	4	IFX	25.5±10.3	60.5±10	25	/	/		28.5±8.3	30.8± 15.2	30.3± 14.8	19.8± 8.7	/		none	0	/	3
Fotiadou, C. et al. (2011)[II]	Greece	1	IFX	10	48	100	6-24	20.2	1/1	25	30	31	40	0	0	none	0	/	3
Navarro, R. et al. (2013)[II]	Spain	1	IFX	37	36	100	25*	22.2	0	42	52	64	62	0	0	LAM[2]	0	none	3
Ozcelik, S. et al. (2020)[II]	Türkei	6	IFX	24±10.7	58.2±10.8	33.3	/	/	/	22.3±4.8	23.3±3.1	24.6±10.6	23±10.5	0	1	LAM[1] (1/6) none (5/6)	1/6	/	3
Chularojanamontri, L. et al. (2020)[II]	Thailand	1	IFX	3	57	0	/	/	/	/	/	/	/	0	0	none	0	/	3
MTX																			

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
Tang, K. T. et al. (2018)[II]	Taiwan	370	MTX	/	42.6±13.2	28	50.4 ±38.4	/		/				/		48/370	/	Liver cirrhosis (15/370)[3]	3
Chularojanamontri, L. et al. (2020)[II]	Thailand	6	MTX	27±30.1 / = 1/6	56±8.2	66.7	/	/	/	/	/	/	/	3/6 / = 2/6	2/6 / = 1/6	LAM[1](3/6) none (3/6)	2/6 / = 1/6	/	3
SEC																			
Chiu H. Y. et al. (2018)[I]	Taiwan	25	SEC	7.7 ± 3.8	49.7 ± 8.6	16	9.1 ± 3.9	13.4 ± 8.2	/	/		43.7±42.2	/	/		3/25[1]	6/25	Hepatic cancer	2; RoB high
		24		8.7 ± 3.7	54.7 ± 13.4	25	9.2 ± 3.7	20.1 ± 8.3				41.1 ± 28.0				11/24[1]	1/24	/	
Siegel, S. A. R. et al. (2017)[II]	USA	2	SEC	/	/	/	/	/		/				/		2	0	/	3
Ozcelik, S. et al. (2020)[II]	Turkey	1	SEC	12	45	0	/	/	/	37	25	26	28	0	0	none	0	/	3
Galluzzo, M. et al. (2019)[II]	Italy	5	SEC	at least 3.5	/	/	/	/	"complete clearance" 5/5	/	/	/	/	/	"no loger detectable"	2/5[1]	0	/	3
Megna et al. (2022)[II]	Italy	13 HBsAg positive	SEC	53.5 ± 37.5 weeks, Range: 16–	59.3 ± 9.1[$]	25/60 (41.7 %)[$]	/	/	/	31.4 ± 15.8 (IU/L)[$]	/	27.9 ± 18.6 (IU/L)[$]	/	/	/	LAM (12) ENT (1)	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
		19 HBcAb positive		240 weeks												LAM (1) ENT (1)	1		
Qin et al. (2022)[II]	China	4 with chronic inactive HBV infetion [HBsAg (+), HBeAg (-)]	SEC	≥24 weeks	43.7 ± 13.5	30	24 weeks	IGA: - clear / almost clear: 5% - mild: 25% - moderate / severe: 70% DLQI: - none:	PASI-75: 100% PASI-90: 90% PASI-100: 63% IGA: - clear / almost clear: 90% - mild: 10% -	32.3 ± 20.7 (IU/L)	23 ± 1.2 (IU/L)	41 ± 29.7 (IU/L)	29.3 ± 6.4 (IU/L)	<500 IU/mL	/	ENT (2) none (2)	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
		2 with occult HBV infection [HBsAg (-), HBsAb (-), HBcAb (+)]						0% - small: 10% - moderate / very large / extremely large: 90%	moderate / severe: 0% DLQI: - none: 75% - small: 20% - moderate / very large / extremely large: 5% Mean improvement of: PASI: −13.35 ± 7.41 % BSA affected: −17.11 ± 17 IGA: −2.55 ± 0.94 DLQI: −12.3 ±	31 ± 7 (IU/L)	30 ± 5 (IU/L)	41.5 ± 1.5 (IU/L)	44 ± 1 (IU/L)	<500 IU/mL	/	ENT (1) none (1)	0	/	
		14 with resolved HBV infection [HBsAg (-), HBsAb (+), HBcAb (+)]								21.6 ± 7.8 (IU/L)	22.9 ± 13.7 (IU/L)	27.4 ± 22.5 (IU/L)	29.4 ± 38.6 (IU/L)	<500 IU/mL (10) <20 IU/mL (4)	/	none	0	hepatitis (1)	

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
									7.39 Nota bene: different numbers reported in the text and in Fig. 3 for mean improvement in DLQI										
UST																			
Ting, S. W. et al. (2018)[I]	Taiwan	54	UST	/	47*	16.7	24*	/		"none had liver failure"						ENT[1] (1/54) LAM[2] (1/54)	3/48	/	3
Hsieh, T. Y. et al. (2018)[II]	Taiwan	75	UST	/	/	/	24.7*	/		/				/		unknown[2] (2/75)	2/75	/	3
Chiu, H.Y. et al. (2013)[II]	Taiwan	14	UST	9.4±9	45.5±7.6	28.6	10.4*	/	5/14	"unchanged"				/	"increased" (4/14)	ENT[2] (4/14)	2/14	/	3
Piaserico, S. et al. (2017)[II]	Italy	5	UST	57.2±13.9	55.4±16.5	20	57	/		28.8±11.6	31.8±7.9	31.2±16.2	41.8±19	0	0	LAM[1] (4/5)	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
Navarro, R. et al. (2013)[II]	Spain	1	UST	7	56	0	25*	17.6	1/1 PASI50	32	16	35	15	1/1	0	ENT[2]	0	none	3
Ozcelik, S. et al. (2020)[II]	Turkey	1	UST	24	43	0	/	/	/	18	21	37	27	0	0	LAM[1]	0	/	3
Siegel, S. A. R. et al. (2019)[II]	USA	10	UST	/	47.7±13.5	30	/	BSA 20.1±16.6	BSA 3.2±4.2	/	/	/	"no significant elevation" **	5/10 / = 5/10	3/10 / = 7/10	/	0	/	3
Klujszo et al. (2022)[II]	Poland	5	UST	82.4 (28, 96) weeks[$]	n.r., Range: 54-75	60	75.2 (31, 176) weeks[$]	n.r., Range: 18.4-24	/	/	/	/	/	undetectable	undetectable	/	0	/	3
> than one treatment																			
Cassano N. et al. (2010)[II]	Italy	62	ETA (44) ADA (10) IFX (8)	27.8* 19* 28.8*	54*	32.3	55	15.3 (10.2-39.9)	/	"normal value"				"undetectable"		LAM[2] (1/62)	0	/	3
Morisco, F. et al. (2014)[II]	Italy	23	ADA, ETA, UST,	/	66±10.6	56.5	/	/		/	"unchanged"	27±2.3	"unchanged"	0	0	none	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
		36	IFX, MTX, CsA		52±12.4	25						24±3.2							
Al Mutairi, N. and Abouzaid, H.A. (2018)[I]	Kuwait	28	ADA (11) ETA (10) UST (8)	14.7±12.3 21.7±5.3 30±14.7	51±13.2	10.7	41.4 ±21.4	14.2±1.5	28/28	22 (17–25.8)	23 (12.3–28.8)	21 (17.1–26.4)	23 (14.7–25.3)	0		none	0	none	2; RoB high
		4	ADA (3) ETA (4) UST (1)	15.4±11.7 18.5±23.6 28±11.9	49±15.6	25			4/4							LAM[2] (4/4)			
Pereira, R.et al. (2018)[II]	Portugal	26	ETA (12) ADA (8) IFX (6) > 1 (13)	37.2 50.4 58.8 /	52.7±14.1	38.5	43.6 ±28.7	/		/				"undetectable"		/	0	/	3
Sanz-Bueno, J. (2015)[II]	Spain	20	ADA (13) ETA (7) UST	13 16 18 22	/	25	40*	/		"unchanged"				0	0	none	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
			(6) IFX (7)																
Snast, I. et al. (2017)[II]	Israel	16	ETA (16), ADA (14), IFX (5), UST (12), SEC (3), GOL (1), ALE (1)	70.8±32.4	55.2±11.4	31.3	63.7*	23.3±8.6 BSA 50 (5/16) BSA 70 (1/16)	9/16 PASI50	22.7±5.6	21.9±8.3	21.5±7	19.3±10.7	0	0	LAM[2] (1/16)	0	respiratory infection (1/16), myocardial infarction (1/16) erythema (2/16)	3
Ozcelik, S. et al. (2020)[II]	Turkey	7	ADA (5) ETA (2) IFX (7) SEC (3) UST (1)	65.7±38.2	57.3±12.4	42.9	/	/	/	23.1±6.8	32.9±21.1	24.4±14.9	30±20.4	0	0	LAM[1] (1/7) none (6/7)	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
Chularojanamontri, L. et al. (2020)[II]	Thailand	10	Acitritin (8) CsA (8) ETA (3) IFX (3) MTX (6)	/	51.5±10.9	18.2	/	/	/	/	/	/	/	/	/	/	1/10 / = 4/10	/	3
Chiu, H.Y. et al. (2021)[II]	Taiwan	359 n.r. for each heaptitis B infection	ADA ETA GOL SEC UST	number of treatment episodes: 210	47.6 ± 9.4	20.5	3012 person-months	PASI: 16.8 ± 8.9	Mean PASI improvement (%): 75.1 ± 21.6	/	/	42 ± 65 IU/L	/	99034.5 ± 564964.4 IU/mL	/	51 (24.2%) LAM 3/51 (5.8%) ENT 40/51 (78.4%) TELB 8/51 (15.6%) TEN 2/51 (3.9%)	Chronic HBV: 72/210 (34.3%)	/	3
				number of treatment episodes: 93	54.3 ± 10.5	24.7	1265 person-months	PASI: 19.2 ± 9.3	Mean PASI improvement (%): 76.2 ± 18.7			28 ± 20 IU/L		4.4 ± 8.2 IU/mL		0 (0%)	Occult HBV infection: 3/93 (3.2%)		

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean ±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events	Oxford Level of Evidence
				number of treatment episodes: 258	50.6 ± 11.5	22.5	4532 person-months	PASI: 22.9 ±12.7	Mean PASI improvement (%): 78.5 ± 18.5			33 ± 25 IU/L		1.3 ± 5.8 IU/mL		0 (0%)	Resolved HBV: 13/258 (5.0%)		
Gargiulo et al. (2022)[II]	Italy	17	ADA (1) BRO (1) ETA (1) IXE (2) RIS (10) SEC (2) TIL (2) UST (2)	/	Median: 57, Range: /	29.41	Mean: /, Range: 52-208 weeks	Median: 15, Range: 10-32	PASI-100: 12/17 (70.59%) PASI-90: 15/17 (88.24%)	/	/	/	/	undetectable	/	none	0	/	3

Abbreviation:
/ = data not applicable or reported
1 = before treatment; 2 = while treatment; 3 = no diffrence in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospectice study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; $ = refers to all patients in the study population
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BRO = Brodalumab; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; EFA = Efavirenz; GOL = Golimumab; HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; IXE = Ixekizumab; LAM = Lamivudine; MTX = Methotrexate; TEN = Tenofovir; TELB / LTD = Telbivudine; PASI = Psoriasis Area Severity Index; RIB = Ribavirin; RIS = Risankizumab; SAE = Severe Adverse Event; SEC = Secukinumab; TIL = Tildrakizumab; UST = Ustekinumab
yellow = new study updates 2021 and 2022

Table 5: Hepatitis C

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HcV reactivation (n)[4]	other adverse events	Oxford level of evidence
		Acitretin																	
Chularojanamontri, L. et al. (2021)[II]	Thailand	1	Acitretin	3	44	0	/	/	/	65	177	91	301	/	/	0	no worsening of HCV infection during psoriasis treatment'	/	3
		ADA																	
Piaserico, S et al. (2017)[II]	Italy	20	ADA	40*	49.8±11.3	30	/	15.8±6.2	14/20	39.5±21.2	53.9±32.7	38±20.7	57.3±36.4	16/20	↓ 7/16 (0.7±0.3) ↑ 9/16 (8.8±17.1)	RIB[1] (1/20) IFN/RIB[1] (1/20)	0	/	3
Navarro, R. et al. (2013)[II]	Spain	1	ADA	2	65	0	/	15.6	0/1	20	30	34	55	1/1	↑ (1.03)	none	0	Stroke (1/1)	3
Narcisi, A. et al. (2020)[II]	Italy	6	ADA	17±59	58±5.0	50	/	17.5±6.75	PASI100 (5/6) PASI75(1/6)	63.8±17.6	"no worsening"	57.5±16.0	"no worsening"	1/6	"no worsening"	0	0	no SAE	3
		CsA																	

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HcV reactivation (n)[4]	other adverse events	Oxford level of evidence
Chularojanamontri, L. et al. (2021)[II]	Thailand	1	CsA	24	60	0	/	/	/	96	82	59	73	/	/	/	no worsening of HCV infection during psoriasis treatment'	/	3
ETA																			
Navarro, R. et al. (2013)[II]	Spain	12	ETA	15.5±5.9	51.5±12.8	16.7	/	17.8±8.8	6/12	82.8±42.2	61.9±31	88.1±40.9	53.1±22.5	6/12	↓ 4/6 (0.04±0.08) ↑ 2/6 (8.2±12)	IFN/RIB[2] (3/12)	0	Respratory infection (1/12) HCC (2/12)	3
Garavaglia, M.C. et al. (2010)[II]	Italy	5	ETA	15.6±7.1	59±10.7	20	7-24	22.9±3.2	4/5	42.8±14.1	43±23.6	49±10.5	52.4±37.7	4/5	↓ 3/4 (0.64±0.5) ↑ 1/4 (1.22)	IFN/RIB[2] (1/5)	0	/	3
Di Nuzzo, S. et al. (2013)[II]	Italy	5	ETA	12*	60*	0	/	/		"increased" (2/5)				"unchanged"		/	0	HCC (1/5)	3
Snast, I. et al. (2017)[II]	Israel	3	ETA	18±9.6	57±16.6	0	22.3 (8-36)	19.5±6.7	2/3	48.3±7.6	53.7±18.6	58.7±5.7	72.3±22.9	3/3	↓ 1/3 (0) ↑ 2/3 (1.93±0.93)	none	0	none	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HcV reactivation (n)[4]	other adverse events	Oxford level of evidence
MTX																			
Tang, K. T. et al. (2018)[II]	Taiwan	174	MTX	/	50.4±12.6	36	57.6±4.2	/		/		/		/		42/174	/	Liver cirrhosis (19/174)[3]	3
Chularojanamontri, L. et al. (2021)[II]	Thailand	4	MTX	43±61.5	62.8±12.8	25	/	/	/	30.8±17.1	30.3±17.8	27.5±19.7	33±20.1	1/4 / = 3/4	/	pegIFN/RIB[2] (1/4) / = 3/4	no worsening of HCV infection during psoriasis treatment'	/	3
SEC																			
Chiu, H. Y. et al. (2018)[I]	Taiwan	14	SEC	8.6 ± 3.4	53.9 ± 12.7	14.3	9.0 ± 3.9	/	"Improvement in PASI": 77.7 ± 18.5	/		48.4 ± 50.1	"no significant differences"	/	"no significant differences"	IFN/RIB[1] (4/14) DAA[2] (1/14)	1	HCC	2; RoB high
Siegel, S. A. R. et al. (2017)[II]	USA	3	SEC	/	54-64	/	/	/		"no evidence of significant elevations"				/		/	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HcV reactivation (n)[4]	other adverse events	Oxford level of evidence
Megna et al. (2022)[II]	Italy	30	SEC	53.5 ± 37.5 weeks, Range: 16–240 weeks	59.3 ± 9.1 [$]	25/60 (41.7 %)[$]	/	/	/	31.4 ± 15.8[$]	/	27.9 ± 18.6 (IU/L)[$]	/	undetectable	1 2,000,000 copies/mL	none	1	/	3
UST																			
Chiu, H.Y. et al. (2013)[II]	Taiwan	4	UST	8±2.6	64.8±12.1	0	9.5*	/	0/4	"slightly increased" (3/4)				/	"increased" (3/4)	none	1	HCC (1/4)	3
Siegel, S. A. R. et al. (2019)[II]	USA	11	UST	/	54.3±5.8	27.3	/	BSA 36.5±20.3	BSA 10.8±9.6	/	/	/	no significant elevation** 11/11	7/11 / = 4/11	no significant increase** / = 3/11	3/11[2]	1***	/	3
> than one treatment																			

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HcV reactivation (n)[4]	other adverse events	Oxford level of evidence
Morisco, F. et al. (2014)[II]	Italy	15	ADA, ETA, UST, IFX	/	62±11.8	20	48	/		/	/	25	"unchanged"	/	"unchanged"	none	0	/	3
Al Mutairi, N. and Abouzaid, H.A. (2018)[I]	Kuwait	7	ADA (7) ETA (1)	13.7±10.4 20	54±12.9	40	41.4±21.4	/	7/7	22 (17–25.8)	21 (17.1–26.4)	23 (12.3–28.8)	23 (14.7–25.3)	"detectable level" (2/4)	"detectable level" (2/4)	/	0	none	2; RoB high
Prignano, F. et al. (2011)[II]	Italy	5	ADA (2) ETA (3)	6 8.6	50.4*	25	7.3	/		"unchanged"				"unchanged"		none	0	/	3
Navarro, R. et al. (2013)[II]	Spain	5	ADA (3) ETA (5) UST (1) IFX (1)	6.7±3.8 15.6±16.2 17 8	39.8±11.3	0	/	14.6±8.3	2/5	110±78.9	145±114.7	106.6±68.1	107.9±46.1	2/5	↓ 1/2 (0) ↑ 1/2 (1.57)	none	0	none	3
Snast, I. et al. (2017)[II]	Israel	1	ETA ADA	36	78	0	22.3*	BSA 50	1/1	68	32	74	32	/		none	0	none	3
Chularojanamontri, L. et al. (2021)[II]	Thailand	3	Acitretin (3) CsA (2) ETA (1) IFX (1)	/	52.7±6.4	33.3	/	/	/	46.6±27,8	27±21.7	43±30.6	14.7±4.9	1/3 / = 2/3	/	pegIFN/RIB[2] 1/3 / = 2/3	no worsening of HCV infection during psoriasis	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HcV reactivation (n)[4]	other adverse events	Oxford level of evidence
			MTX (1)														treatment'		
Chiu, H.Y. et al. (2021)[II]	Taiwan	61	ADA ETA GOL SEC UST	number of treatment episodes: 112	53.1 ± 11.9	17.9	1522 person-months	18.5 ± 7.6	Mean PASI improvement (%): 75.2 (± 23.0)	/	/	47 ± 44 (IU/L)	/	2660887.6 ± 7554939.7 (IU/mL)	/	14/112 (12.5%)[§]	14/112 (12.5%)	/	3
Gargiulo et al. (2022)[II]	Italy	4	ADA (1) BRO (1) IXE (1) RIS (1) SEC (1) UST (1)	/	Median.: 54.5, Range: /	25	Mean: /, Range: 52-220 weeks	Mean: /, Range: 10-30	PASI-100: 2/4 (50%)	/	/	/	/	undetectable	/	/	0	/	3

								Severity score (e.g. PASI)		Transaminasis				Viral load					
										AST mean±SD		ALT mean±SD							
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean± SD	Age (Y) mean± SD	♀ (%)	Eof (M) mean±SD	Baseline mean± SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HcV reactivation (n)[4]	other adverse events	Oxford level of evidence

Abbreviation:

/ = data not applicable or reported

1 = before treatment; 2 = while treatment; 3 = no difference in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow

I = prospectice study; II = retrospective study

* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported; § = Patients with HCV who had received antiviral drugs before or concurrently with biologics; $ = refers to all patients in the study population

ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; DAA = Direct acting antivirals; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; EFA = Efavirenz; GOL = Golimumab; HCC = Hepatocellular Carcinoma; HCV = Hepatitis C Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; TEN = Tenofovir; PASI = Psoriasis Area Severity Index; PegIFN = Pegylated Interferon; RIB = Ribavirin; SAE = Severe Adverse Event; SEC = Secukinumab; UST = Ustekinumab

yellow = new study updates 2021 and 2022

Appendix

Table 6: Search strategy for the review update on psoriasis and viral hepatitis

Databases: Embase Classic+Embase 1947 to 2022 October 26

Ovid MEDLINE(R) ALL 1946 to October 26, 2022

1	exp psoriasis/ or psoria*.mp.
2	pustulosis palmaris et plantaris.ti,ab.
3	(pustulosis and palm and soles).ti,ab.
4	palmoplantar* pustulosis.ti,ab.
5	1 or 2 or 3 or 4
6	urea/ or urea*.mp.
7	uric acid.mp. or uric acid/
8	salicyl* acid.mp. or salicylic acid/
9	calcineu* inhibito*.mp. or calcineurin inhibitors/
10	tacrolimus/ or pimecrolim*.mp.
11	dithranol*.mp. or anthralin/
12	cortisone/ or cortiso*.mp.
13	betamethasone/ or betametha*.mp.
14	mometaso*.mp. or glucocorticoids/ or mometasone furoate/
15	retinoids/ or tazarot*.mp.
16	coal tar.mp. or coal tar/
17	vit d3.mp or cholecalciferol/
18	calcipotrio*.mp.
19	tacalcito*.mp.
20	calcitriol/ or calcitrio*.mp.
21	phototherap*.mp. or exp phototherapy/
22	puva therapy/ or photochemotherapy/ or puva.mp.
23	exp ultraviolet therapy/ or uv-b therap*.mp.
24	photodynamic therap*.mp.
25	photochemotherap*.mp.
26	light therap*.mp.
27	photoradiation therap*.mp.
28	bbuvb.mp.
29	nbuvb.mp.
30	bb-uvb.mp.
31	nb-uvb.mp.
32	broad band uvb.mp.
33	broad band ultraviolet.mp.
34	narrow band uvb.mp.
35	narrow band ultraviolet.mp.
36	psoralen ultraviolet a.mp.
37	psoralen uva.mp.
38	laser therap*.mp. or laser therapy/
39	ciclospori*.mp. or cyclosporine/
40	cyclospor*.mp.
41	fumar*.mp. or exp fumarates/
42	fumaderm.mp.
43	dimethylfumara*.mp.
44	fae.ti,ab.
45	dmf.ti,ab.
46	exp methotrexate/ or mtx.mp.
47	methotrexa*.mp.
48	amethopterin.mp.
49	mexate.mp.
50	acitretin.mp. or acitretin/
51	retinoids/
52	phosphodiesterase 4 inhibitors/ or apremilast.mp.
53	(etanercep* or enbrel).mp. or etanercept/
54	(infliximab* or remicade).mp. or infliximab/
55	ustekinumab.mp. or ustekinumab/
56	cnto 1275.mp.
57	stelara.mp.
58	secukinumab.mp.
59	guselkumab.mp.

60	adalimumab*.mp. or adalimumab/
61	(d2e7 or humira).mp.
62	exp antibodies, monoclonal/
63	monoclonal antibod*.mp.
64	exp interleukin-23/ or exp interleukin-12/
65	brodalumab.mp.
66	ixekizumab.mp.
67	risankizumab.mp.
68	tildrakizumab.mp.
69	certolizumab.mp.
70	bimekizumab.mp.
71	deucravacitinib.mp.
72	(tumor necrosis factor-alpha or tumour necrosis factor-alpha).mp.
73	anti tnf.mp.
74	(tumor necrosis factor antibod* or tumour necrosis factor antibod*).mp.
75	(antitumor necrosis factor or antitumour necrosis factor).mp.
76	(anti tumor necrosis factor or anti tumour necrosis factor).mp.
77	(tnf antibod* or tnf alpha antibod*).mp.
78	climate therap*.mp. or climatotherapy/
79	psychotherapy/ or psychosocial therap*.mp.
80	exp tumor necrosis factor-alpha/
81	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80
82	5 and 81
83	exp hepatitis/ or hepatit*.mp.
84	chronic hepatit*.mp. or exp hepatitis, chronic/
85	hepatitis b/ or hepatit* b.mp.
86	hbv.ti,ab.
87	hepatitis c, chronic/ or hepatitis c/ or hepatit* c.mp.
88	non a non b hepatit*.mp.
89	hcv.ti,ab.
90	hepati* d.mp.
91	hepatitis a/ or hepatit* infection.mp.
92	hav.ti,ab.
93	83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92
94	82 and 93

Additional time filters:

("202106*" or "202107*" or "202108*" or "202109*" or "202110*" or "202111*" or "202112*" or "2022*").dc. (Embase)

("202106*" or "202107*" or "202108*" or "202109*" or "202110*" or "202111*" or "202112*" or "2022*").dt. (Medline)

Table 7: Search strategy for the review update on psoriasis and viral hepatitis

Databases: Embase Classic+Embase 1947 to 2022 October 26

Ovid MEDLINE(R) ALL 1946 to October 26, 2022

1	exp psoriasis/ or psoria*.mp.
2	pustulosis palmaris et plantaris.ti,ab.
3	(pustulosis and palm and soles).ti,ab.
4	palmoplantar* pustulosis.ti,ab.
5	1 or 2 or 3 or 4
6	deucravacitinib.mp.
7	5 and 6
8	exp hepatitis/ or hepatit*.mp.
9	chronic hepatit*.mp. or exp hepatitis, chronic/
10	hepatitis b/ or hepatit* b.mp.
11	hbv.ti,ab.
12	hepatitis c, chronic/ or hepatitis c/ or hepatit* c.mp.
13	non a non b hepatit*.mp.
14	hcv.ti,ab.
15	hepati* d.mp.
16	hepatitis a/ or hepatit* infection.mp.
17	hav.ti,ab.
18	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19	7 and 18

Additional time filters:

("202101*" or "202102*" or "202103*" or "202104*" or "202105*").dc. (Embase)
("202101*" or "202102*" or "202103*" or "202104*" or "202105*").dt. (Medline)

Table 8: Excluded full-texts for the review update on psoriasis and viral hepatitis

Reference	Reason for exclusion
Babuna Kobaner G, Polat Ekinci A, Kutlay A. Long-term efficacy and safety of ustekinumab for moderate-to-severe psoriasis: A 9-year real-life experience from a tertiary referral center in Turkey. Dermatol Ther. 2021;34(4) (no pagination).	Off topic
Chularojanamontri L, Nimanong S, Wongpraparut C, Silpa-Archa N, Chaiyabutr C, Charoenpipatsin N. How do we treat psoriasis patients with hepatitis C infections in real-world situations? A retrospective analysis of 34 patients. Journal of Dermatological Treatment. 2021;32(3):321-7.	Off topic
Fidan S, Capkin E, Arica DA, Durak S, Okatan IE. Risk of hepatitis B reactivation in patients receiving anti-tumor necrosis factor-alpha therapy. International Journal of Rheumatic Diseases. 2021;24(2):254-9.	Off topic
Hung MH, Tien YC, Chiu YM. Risk factors for losing hepatitis B virus surface antibody in patients with HBV surface antigen negative/surface antibody positive serostatus receiving biologic disease-modifying anti-rheumatic drugs: a nested case-control study. Advances in Rheumatology. 2021;61(1) (no pagination).	No relevant outcomes
Munera-Campos M, Vilar-Alejo J, Rivera R, Carrascosa JM, Dauden E, Herrera-Acosta E, et al. The risk of hepatic adverse events of systemic medications for psoriasis: a prospective cohort study using the BIOBADADERM registry. Journal of Dermatological Treatment. 2022;33(4):2110-7.	No relevant outcomes
Nguyen HT, Pham NTU, Tran TNA, Nguyen NTT, Vu TTP. Secukinumab Demonstrated High Effectiveness in Vietnamese Patients with Moderate-To-Severe Plaque Psoriasis in a Real-World Clinical Setting: 16 Week Results from an Observational Study. Dermatol Ther (Heidelb). 2021;11(5):1613-21.	No relevant outcomes
Ozaki S, Ichiyama S, Ito M, Hoashi T, Kanda N, Saeki H. Real-world blood examination screening data before initiation of biologics for psoriasis patients. J Dermatol. 2022;49(5):534-8.	Off topic

Update 1

Summary of methods and results (August 2021)

Authors: M. Kinberger, R. Jakubzyk

Update 1 – August 2021 (blue = new study or additional data)

What was the aim of this systematic review?

The aim of this review update was to continuously inform the guideline development group of new evidence on patients with psoriasis vulgaris and coexisting viral hepatitis.
Many systemic psoriasis treatments modulate immune functions and can reactivate hepatitis, and are known to cause liver injury. However, patients with severe psoriasis and viral hepatitis still need systemic treatment. In this systematic review we investigated the safety and efficacy of systemic psoriasis treatment options for patients with concomitant viral hepatitis.

What did we do?

Two databases were searched systematically. We only included studies with patients treated with systemic psoriasis therapies who also had viral hepatitis B or C. We assigned Levels of Evidence for all studies included using the Center of Evidence Based Medicine Oxford recommendations and RoB 2.0 tool [4] for the randomized trials. For details, see Methods Report.

What are the main results of the review?

We found 3 prospective studies, 2 register study and 23 retrospective studies with 1230 patients with psoriasis vulgaris and coexisting viral hepatitis (hepatitis B n=930; hepatitis C n=300).

<u>Hepatitis B</u>

- Prospective data
    - In a study by Chiu et al. 49 patients with psoriasis and hepatitis B were treated with secukinumab. A reactivation of hepatitis B was reported in 7 of 49 (14.3%) patients (risk of bias high).
    - In a cohort study Ting et al. reported hepatitis B reactivation in 3 of 48 (6.3%) patients with isolated anti-HBc or resolved HBV infection treated with ustekinumab (Oxford Level of Evidence 3).
    - Al Mutairi and Abouzaid reported that of 32 patients treated with biologics (ADA, ETA, UST), none suffered from hepatitis reactivation, an increase in transaminases or viral load. A PASI75 response was reported in all 32 patients (risk of bias high).
- Retrospective data
    - Acitretin
        - Chularojanamontri et al. reported that viral reactivation did not occur in 9 patients treated with acitretin.
    - CsA
        - Chularojanamontri et al. reported that viral reactivation did not occur in 2 patients treated with ciclosporin.
    - MTX
        - Tang et al. reported that 15 of 370 (4.1%) hepatitis B patients treated with MTX developed liver cirrhosis.

        - Chularojanamontri et al. reported that 2 of 6 (33.3%) patients treated with MTX suffered from viral reactivation.
    - TNFi
        - ADA: A total of 8 studies with 38 patients reported no hepatitis B reactivation in patients treated with adalimumab. A total of 3 studies with 29 patients reported a PASI75 response in 28 (96.6%) patients treated with adalimumab.
        - ETA: A total of 8 studies with 43 patients reported hepatitis B reactivation in 3 (7.0%) patients treated with etanercept. A total of 3 studies with 14 patients reported at least a PASI50 response in 13 (92.9%) patients treated with etanercept.
        - IFX: A total of 5 studies with 13 patients reported a hepatitis B reactivation in 1 (7.7%) patient treated with infliximab. A total of 2 studies with 2 patients reported a PASI75 response in 1 (50%) patient treated with infliximab.
    - UST
        - A total of 6 studies with 106 patients reported a hepatitis B reactivation in 4 (3.8%) patients treated with ustekinumab. One study reported a PASI75 response in 5 of 14 (35.7%) patients.
    - SEC
        - A total of 3 studies with 8 patients reported that viral reactivation did not occur in patients treated with secukinumab. One study with 5 patients reported a "complete clearance" of psoriasis lesions in all 5 patients.
    - More than one treatment
        - A total of 7 studies with 200 patients treated with more than one drug (conventional and biologics) reported a hepatitis B reactivation in 1 (0.5%) patient.

<u>Hepatitis C</u>

- Prospective data
    - In a study by Chiu et al. 14 patients with psoriasis and hepatitis C were treated with secukinumab. A reactivation of hepatitis C was reported in 1 of 14 (7.1%) patients (risk of bias high)
    - Al Mutairi and Abouzaid reported that of 7 patients treated with TNFi (ADA, ETA), none sufferd from hepatitis reactivation, an increase in transaminases or viral load. A PASI75 response was reported in all 7 patients (risk of bias high).
- Retrospective data
    - Acitretin
        - Chularojanamontri et al. reported "no worsening of HCV infection" during acitretin treatment in 1 patient with psoriasis vulgaris and hepatitis C.
    - CsA
        - Chularojanamontri et al. reported "no worsening of HCV infection" during ciclosporin treatment in 1 patient with psoriasis vulgaris and hepatitis C.
    - MTX
        - Tang et al. reported that 19 of 174 (10.9%) hepatitis C patients treated with MTX developed liver cirrhosis.
        - Chularojanamontri et al. reported "no worsening of HCV infection" during MTX treatment in 4 patients with psoriasis vulgaris and hepatitis C.
    - TNFi

- ADA: A total of 3 studies with 27 patients reported no hepatitis C reactivation in patients treated with adalimumab. In 20 of 27 (74.1%) patients, a PASI75 response was reported.
- ETA: A total of 4 studies with 25 patients reported no hepatitis C reactivation in patients treated with etanercept. A total of 3 studies with 20 patients reported a PASI75 response in 12 (60%) patients treated with etanercept.

- UST
  - A total of 2 studies with 15 patients reported hepatitis C reactivation in 2 (13.3%) patients treated with ustekinumab.
- SEC
  - Siegel et al. reported zero HCV reactivation in 3 patients treated with SEC.
- More than one treatment
  - A total of 5 studies with 29 patients reported zero cases of hepatitis C reactivation in patients treated with more than one systemic drug (conventional and biologics).

Key message

Hepatitis B reactivation was reported in 21 of 555 patients who received systemic psoriasis treatment. Hepatitis C reactivation was reported in 3 of 126 patients who received systemic psoriasis treatment. Neither in patients with hepatitis B nor in patients with hepatitis C has virus reactivation been reported during treatment with acitretin (n=10), ciclosporin (n=3) or adalimumab (n=65). Etanercept (n=25) and MTX (n=4) also did not lead to virus reactivation in hepatitis C patients in the included studies. Very few retrospective studies are available. The reporting on whether patients have also received antiviral treatment during psoriasis therapy is inconsistent or incomplete. In addition, the antigen and antibody status of hepatitis B patients is reported inconsistently, hence further differentiation by status is not possible. Transaminases levels almost remained stable in the reported studies.

In 64 of 81 (79.0%) patients with psoriasis vulgaris and hepatitis B or C treated with TNFi a PASI75 response was reported in retrospective studies. Prospective data was only in one study available in which all patients (n=32) with psoriasis vulgaris and hepatitis B showed a PASI75 response after a treatment with ADA, ETA or UST (risk of bias high). However, a direct comparison with non-hepatitis patients is missing.

How up-to-date is this review?

We searched for studies that has been published up to 2 July 2021

Inclusion criteria

Apart from the newly included drugs bimekizumab, certolizumab pegol, risankizumab and tildrakizumab we did not change the search strategy and the inclusion criteria of the previous version.

Table 9: Eligibility criteria for the review update on psoriasis and viral hepatitis

Patients	Inclusion: on adult patients with a clinical diagnosis of psoriasis and a concomitant hepatitis B or C being treated for psoriasis Exclusion: patients with psoriatic arthritis only
Intervention	Conventional systemic treatment (acitretin, apremilast, ciclosporin, fumarates, methotrexate) and biologicals (TNFi: adalimumab, etanercept, certolizumab pegol (new), infliximab; anti-IL12/23: ustekinumab; anti-IL17: bimekizumab (new), brodalumab, ixekizumab, secukinumab; anti-IL23: guselkumab, risankizumab (new), tildrakizumab (new)
Comparator	Comparisons with another included drug and/or placebo
Outcomes	Change in skin lesions based on PASI (Psoriasis Area Severity Index) or PGA (Physician Global Assessment) or another study specific assessment. Transaminases, viral load or other study specific outcomes Type and proportion of other adverse events Quality of life based on SF-36 (The Short Form (36) Health Survey), DLQI (Dermatology Life Quality Index) or another study specific assessment.
Study Design	Inclusion: randomized controlled trials, clinical trials (with and without comparison group), cohort studies, case control studies and cross sectional studies Exclusion: case series, case reports

Information sources

The search strategy was updated and the databases MEDLINE Ovid from 1946 and Embase Ovid from 1974 were searched for the period 2019 to 2 June 2021. Furthermore, we examined the reference lists of included studies to identify references to relevant trials. The full search strategy is shown below. We screened all identified abstracts/titles for eligibility. Included titles/abstracts were then screened as full texts based on the above listed eligibility criteria.

Data collection, statistical analysis and evaluation

We performed the screening and did the data extraction using a standardized form. We recorded all full-texts excluded and the primary reason for exclusion (see below).

Methodological quality assessment/ Risk of bias assessment

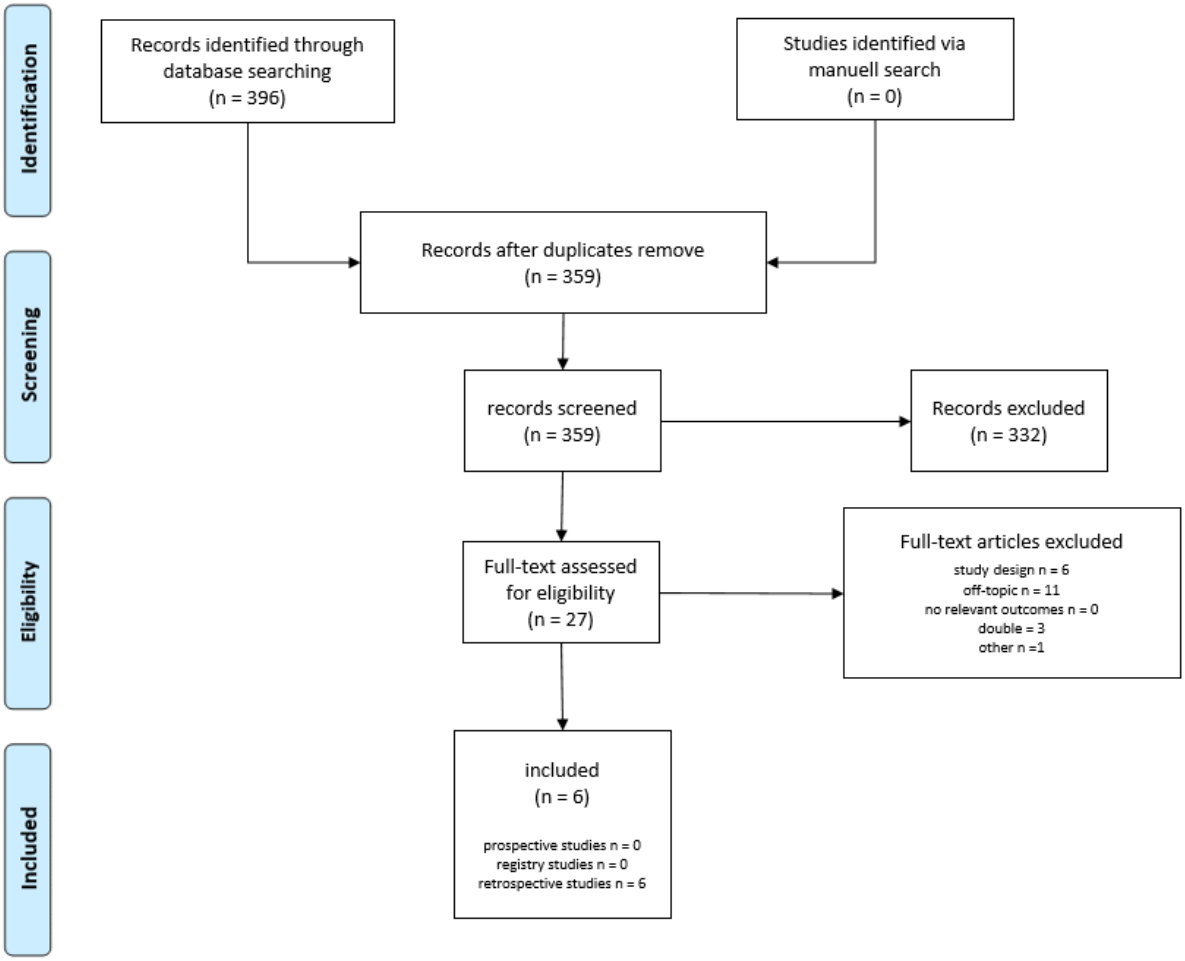
We assigned Levels of Evidence for all studies included using the Center of Evidence Based Medicine Oxford recommendations. To assess risk of bias in randomized trials we additionally used the RoB 2.0 tool [4].

Results

Our update search yielded 396 citations, 6 of which fulfilled the inclusion criteria [31-36] (see study selection flow chart).

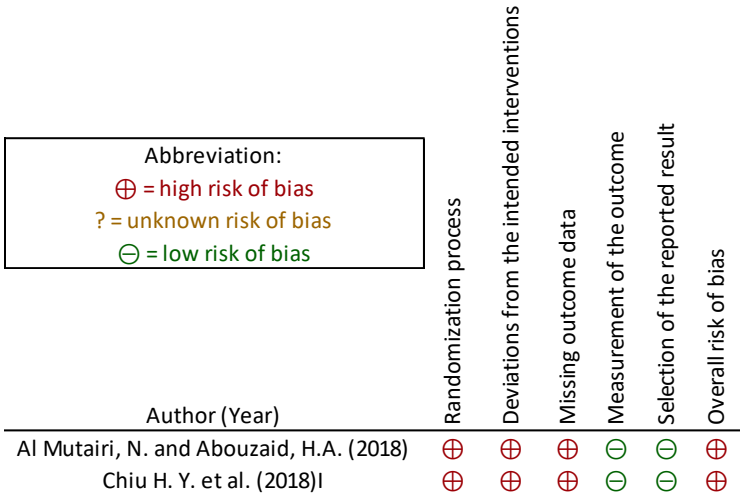
No studies on systemic treatment with apremilast, bimekizumab, certolizumab pegol, brodalumab, fumarates, guselkumab, ixekizumab, risankizumab and tildrakizumab were identified that reported outcomes for viral hepatitis neither in the original search nor in the update.

Figure 3: Study selection flowchart for the selection of studies for the review update on psoriasis and viral hepatitis



Based on the 'Levels of Evidence - Center of Evidence Based Medicine Oxford recommendations' all retrospective studies were categorized level 3. Results of the additional assessment for prospective randomized studies with Risk of Bias Tool 2 (RoB 2) [4] are shown in Table 10. In the update, no further prospective randomized studies were found.

Table 10: Risk of bias in prospective studies (no new data since 2019)



RISK OF BIAS – PROSPECTIVE RANDOMIZED STUDIES

Data for overall 1229 patients with psoriasis and viral hepatitis was extracted. Of those, 929 patients suffered from hepatitis B infection and 300 from hepatitis C infection. The tables below are providing detailed information, sorted by medication used.

Table 11: Hepatitis B

								Severity score (e.g. PASI)		Transaminasis				Viral load				
										AST mean±SD		ALT mean±SD						
Author (Y)	Place	Patients (n)	Drug	Buration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Baseline mean±SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	other adverse events
		Acitretin																
Chularojanamontri, L. et al. (2020)[II]	Thailand	9	Acitretin	20.4 ±25.8	55.8±9.0	11.1	/	/	/	/	/	/	/	5/11	2/11 / = 1/11	none (4/11) LAM/TEN/EFA[2] (1/11) LAM/TEN[2] (1/11) TEN/LAM[2] (1/11) LAM[2] (1/11) LAM/ENT[2] (1/11)	0	/
		ADA																
Piaserico, S et al. (2017)[II]	Italy	17	ADA	27*	50.8±12.5	35.3	/	21.2±6.9	16/17	39±25.4	40.4±25	39.7±27.8	44.9±30.4	0	0	LAM[1] (8/17) LAM/ENT[1] (1/17)	0	/
Fotiadou, C. et al. (2011)[II]	Greece	3	ADA	12±3	53.7± 10.6	33.3	6-24	14.1±2	3/3	19.3±2.1	20.7±1.2	21±2.6	21.3±2.5	0	0	none	0	/
Nosotti, L. et al. (2010)[II]	Italy	3	ADA	9.1±3.7	54±7.2	33.3	/	12.1±13.7	/	13±1.7	18.7±4.2	"unchanged"	"unchanged"	0	0	none	0	/
Navarro, R. et al. (2014)[II]	Spain	2	ADA	11 26	74 68	50	/	/		17 9	19 21	20 14	20 43	/		none	0	/
Snast, I. et al. (2017)[II]	Israel	2	ADA	12 72	55 69	0	63.7*	26.1 BSA 50	2/2 PASI50	35 19	29 34	34 24	42 14	0	0	none	0	Pneumonia (1/2)

Cho, Y.T. et al. (2012)[II]	Taiwan	1	ADA	27	44	0	14	/		15	46	22	34	0	0	none	0	none
Ozcelik, S. et al. (2020)[II]	Turkey	1	ADA	48	55	0	/	/	/	29	22	26	16	0	0	none	0	/
Narcisi, A. et al. (2020)[II]	Italy	9	ADA	20±5.2	59±9.4	44.4	/	18.44±4.14	PASI100 7/9 PASI75 2/9	32.1±16.8	"no worsening"	23.6±19.4	"no worsening"	2/9	"no worsening"	TEN (2/9) LAM (2/9) none (5/9)	0	no SAE
CsA																		
Chularojanamontri, L. et al. (2020)[II]	Thailand	2	CsA	21.5±10.6	43.5±2.1	0	/	/	/	/	/	/	/	2/2	/ = 1/2	LAM[2] (1/2) TEN[2] (1/2)	0	/
ETA																		
Prignano, F. et al. (2011)[II]	Italy	11	ETA	8.6*	61.4*	27.3	7.3	/		"unchanged"				0	0	none	0	/
Snast, I. et al. (2017)[II]	Israel	8	ETA	55.2±46.3	57.3±12.2	37.5	63.7*	19.8±2.7 BSA 50 (4/8)	8/8 PASI50	27.6±16.8	22.2±7.2	24±9.2	19.5±8.5	0	0	LAM[2] (1/8)	0	none
Navarro, R. et al. (2014)[II]	Spain	7	ETA	28.7±20.7	60.6±15.4	28.6	/	/		34.9±14.9	34.7±21.4	44±23.4	32.6±19.6	/		none	0	/
Cho, Y.T. et al. (2012)[II]	Taiwan	6	ETA	24.8±12.7	42.6±4.1	16.7	31.3±13	/		34.5±26.7	35.5±8.2	33.3±24.6	47±28.9	2	2	LAM[2] (1/6) LAM/ENT[2] (1/6)	3/6	none
Nosotti, L. et al. (2010)[II]	Italy	4	ETA	10.5±5.7	51.3±5.7	0	/	7.4±4.6	/	23.5±3.1	28.3±5.7	"unchanged"	"unchanged"	0	0	LAM[2] (1/4)	0	/
Fotiadou, C. et al. (2011)[II]	Greece	3	ETA	12.1±5.9	49.7±14	66.7	6-24	12.1±2.2	3/3	17.3±1.5	18.3±1.5	20.3±3.1	22.7±3.2	0	0	LAM[2] (1/3)	0	/
Navarro, R. et al. (2013)[II]	Spain	3	ETA	27±19	43.7±13	33.3	25*	19.7±4.8	2/3 PASI50	28.3±4	44.3±14.6	46.3±3	45.7±13.7	1	0	ADE/ENT[2] (1/3) LAM[2] (2/3)	0	none

Chularojanamontri, L. et al. (2020)[II]	Thailand	1	ETA	1	70	0	/	/	/	/	/	/	/	/	/	none	0	/
		IFX																
Navarro, R. et al. (2014)[II]	Spain	4	IFX	25.5±10.3	60.5±10	25	/	/		28.5±8.3	30.8± 15.2	30.3± 14.8	19.8± 8.7	/		none	0	/
Fotiadou, C. et al. (2011)[II]	Greece	1	IFX	10	48	100	6-24	20.2	1/1	25	30	31	40	0	0	none	0	/
Navarro, R. et al. (2013)[II]	Spain	1	IFX	37	36	100	25*	22.2	0	42	52	64	62	0	0	LAM[2]	0	none
Ozcelik, S. et al. (2020)[II]	Türkei	6	IFX	24±10.7	58.2±10.8	33.3	/	/	/	22.3±4.8	23.3±3.1	24.6±10.6	23±10.5	0	1	LAM[1] (1/6) none (5/6)	1/6	/
Chularojanamontri, L. et al. (2020)[II]	Thailand	1	IFX	3	57	0	/	/	/	/	/	/	/	0	0	none	0	/
		MTX																
Tang, K. T. et al. (2018)[II]	Taiwan	370	MTX	/	42.6±13.2	28	50.4 ±38.4	/		/				/		48/370	/	Liver cirrhosis (15/370)[3]
Chularojanamontri, L. et al. (2020)[II]	Thailand	6	MTX	27±30.1 / = 1/6	56±8.2	66.7	/	/	/	/	/	/	/	3/6 / = 2/6	2/6 / = 1/6	LAM[1](3/6) none (3/6)	2/6 / = 1/6	/
		SEC																
Chiu H. Y. et al. (2018)[I]	Taiwan	25	SEC	7.7 ± 3.8	49.7 ± 8.6	16	9.1 ± 3.9	13.4 ± 8.2	/	/		43.7±42.2	/	/		3/25[1]	6/25	Hepatic cancer
		24		8.7 ± 3.7	54.7 ± 13.4	25	9.2 ± 3.7	20.1 ± 8.3				41.1 ± 28.0				11/24[1]	1/24	/
Siegel, S. A. R. et al. (2017)	USA	2	SEC	/	/	/	/	/		/				/		2	0	/
Ozcelik, S. et al. (2020)[II]	Turkey	1	SEC	12	45	0	/	/	/	37	25	26	28	0	0	none	0	/

Galluzzo, M. et al. (2019)[II]	Italy	5	SEC	at least 3.5	/	/	/	/	"complete clearance" 5/5	/	/	/	/	/	"no loger detectable"	2/5[1]	0	/
UST																		
Ting, S. W. et al. (2018)[I]	Taiwan	54	UST	/	47*	16.7	24*	/		"none had liver failure"						ENT[1] (1/54) LAM[2] (1/54)	3/48	/
Hsieh, T. Y. et al. (2018)[II]	Taiwan	75	UST	/	/	/	24.7*	/		/				/		unknown[2] (2/75)	2/75	/
Chiu, H.Y. et al. (2013)[II]	Taiwan	14	UST	9.4±9	45.5±7.6	28.6	10.4*	/	5/14	"unchanged"				/	"increased" (4/14)	ENT[2] (4/14)	2/14	/
Piaserico, S. et al. (2017)	Italy	5	UST	57.2±13.9	55.4±16.5	20	57	/		28.8±11.6	31.8±7.9	31.2±16.2	41.8±19	0	0	LAM[1] (4/5)	0	/
Navarro, R. et al. (2013)[II]	Spain	1	UST	7	56	0	25*	17.6	1/1 PASI50	32	16	35	15	1/1	0	ENT[2]	0	none
Ozcelik, S. et al. (2020)II	Turkey	1	UST	24	43	0	/	/	/	18	21	37	27	0	0	LAM[1]	0	/
Siegel, S. A. R. et al. (2019)[II]	USA	10	UST	/	47.7±13.5	30	/	BSA 20.1±16.6	BSA 3.2±4.2	/	/	/	"no significant elevation"**	5/10 / = 5/10	3/10 / = 7/10	/	0	/
> than one treatment																		
Cassano N. et al. (2010)[II]	Italy	62	ETA (44) ADA (10) IFX (8)	27.8* 19* 28.8*	54*	32.3	55	15.3 (10.2-39.9)	/	"normal value"				"undetectable"		LAM[2] (1/62)	0	/
Morisco, F. et al. (2014)[II]	Italy	23	ADA, ETA, UST,	/	66±10.6	56.5	/	/		/	"unchanged"	27±2.3	"unchanged"	0	0	none	0	/

		36	IFX, MTX, CsA		52±12.4	25					24±3.2					
Al Mutairi, N. and Abouzaid, H.A. (2018)[I]	Kuwait	28	ADA (11) ETA (10) UST (8)	14.7±12.3 21.7±25.3 30±14.7	51±13.2	10.7	41.4 ±21.4	14.2±1.5	28/28	22 (17–25.8)	23 (12.3–28.8)	21 (17.1–26.4)	23 (14.7–25.3)	0	none	0	none
		4	ADA (3) ETA (4) UST (1)	15.4±11.7 18.5±23.6 28±11.9	49±15.6	25			4/4						LAM[2] (4/4)		
Pereira, R.et al. (2018)[II]	Portugal	26	ETA (12) ADA (8) IFX (6) > 1 (13)	37.2 50.4 58.8 /	52.7±14.1	38.5	43.6 ±28.7	/		/				"undetectable"	/	0	/
Sanz-Bueno, J. (2015)[II]	Spain	20	ADA (13) ETA (7) UST (6) IFX (7)	13 16 18 22	/	25	40*	/		"unchanged"				0	0	none	0	/
Snast, I. et al. (2017)[II]	Israel	16	ETA (16), ADA (14), IFX (5), UST (12), SEC (3), GOL	70.8±32.4	55.2±11.4	31.3	63.7*	23.3±8.6 BSA 50 (5/16) BSA 70 (1/16)	9/16 PASI50	22.7±5.6	21.9±8.3	21.5±7	19.3±10.7	0	0	LAM[2] (1/16)	0	respiratory infection (1/16), myocardial infarction (1/16) erythema (2/16)

			(1), ALE (1)														
Ozcelik, S. et al. (2020)[II]	Turkey	7	ADA (5) ETA (2) IFX (7) SEC (3) UST (1)	65.7±38.2	57.3±12.4	42.9	/	/	/	23.1±6.8	32.9±21.1	24.4±14.9	30±20.4	0	0	LAM[1] (1/7) none (6/7)	0	/
Chularojanamontri, L. et al. (2020)[II]	Thailand	10	Acitretin (8) CsA (8) ETA (3) IFX (3) MTX (6)	/	51.5±10.9	18.2	/	/	/	/	/	/	/	/	/	/	1/10 / = 4/10	/

Abbreviation:
/ = data not applicable or reported
1 = before treatment; 2 = while treatment; 3 = no diffrence in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospectice study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load;
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; EFA = Efavirenz; GOL = Golimumab; HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; TEN = Tenofovir; PASI = Psoriasis Area Severity Index; RIB = Ribavirin; SAE = Severe Adverse Event; SEC = Secukinumab; UST = Ustekinumab

Table 12: Hepatitis C

								Severity score (e.g. PASI)		Transaminasis				Viral load				
										AST mean±SD		ALT mean±SD						
Author (Y)	Place	Patients (n)	Drug	Buration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Baseline mean±SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Baseline (n)	Eof (n)	Antiviral therapy	HcV reactivation (n)[4]	other adverse events
		Acitretin																
Chularojanamontri, L. et al. (2021)[II]	Thailand	1	Acitretin	3	44	0	/	/	/	65	177	91	301	/	/	0	no worsening of HCV infection during psoriasis treatment'	/
		ADA																
Piaserico, S et al. (2017)[II]	Italy	20	ADA	40*	49.8±11.3	30	/	15.8±6.2	14/20	39.5±21.2	53.9±32.7	38±20.7	57.3±36.4	16/20	↓ 7/16 (0.7±0.3) ↑ 9/16 (8.8±17.1)	RIB[1] (1/20) IFN/RIB[1] (1/20)	0	/
Navarro, R. et al. (2013)[II]	Spain	1	ADA	2	65	0	/	15.6	0/1	20	30	34	55	1/1	↑ (1.03)	none	0	Stroke (1/1)
Narcisi, A. et al. (2020)[II]	Italy	6	ADA	17±59	58±5.0	50	/	17.5±6.75	PASI100 (5/6) PASI75(1/6)	63.8±17.6	"no worsening"	57.5±16.0	"no worsening"	1/6	"no worsening"	0	0	no SAE
		CsA																

Chularojanamontri, L. et al. (2021)[II]	Thailand	1	CsA	24	60	0	/	/	/	96	82	59	73	/	/	/	no worsening of HCV infection during psoriasis treatment'	/
ETA																		
Navarro, R. et al. (2013)[II]	Spain	12	ETA	15.5±5.9	51.5±12.8	16.7	/	17.8±8.8	6/12	82.8±42.2	61.9±31	88.1±40.9	53.1±22.5	6/12	↓ 4/6 (0.04±0.08) ↑ 2/6 (8.2±12)	IFN/RIB[2] (3/12)	0	Respratory infection (1/12) HCC (2/12)
Garavaglia, M.C. et al. (2010)[II]	Italy	5	ETA	15.6±7.1	59±10.7	20	7-24	22.9±3.2	4/5	42.8±14.1	43±23.6	49±10.5	52.4±37.7	4/5	↓ 3/4 (0.64±0.5) ↑ 1/4 (1.22)	IFN/RIB[2] (1/5)	0	/
Di Nuzzo, S. et al. (2013)[II]	Italy	5	ETA	12*	60*	0	/	/		"increased" (2/5)				"unchanged"		/	0	HCC (1/5)
Snast, I. et al. (2017)[II]	Israel	3	ETA	18±9.6	57±16.6	0	22.3 (8-36)	19.5±6.7	2/3	48.3±7.6	53.7±18.6	58.7±5.7	72.3±22.9	3/3	↓ 1/3 (0) ↑ 2/3 (1.93±0.93)	none	0	none
MTX																		
Tang, K. T. et al. (2018)[II]	Taiwan	174	MTX	/	50.4±12.6	36	57.6±4.2	/		/		/		/		42/174	/	Liver cirrhosis (19/174)[3]
Chularojanamontri, L. et al. (2021)[II]	Thailand	4	MTX	43±61.5	62.8±12.8	25	/	/	/	30.8±17.1	30.3±17.8	27.5±19.7	33±20.1	1/4 / = 3/4	/	pegIFN/RIB[2] (1/4) / = 3/4	no worsening of HCV infection during psoriasis	/

																	treatment'	
SEC																		
Chiu, H. Y. et al. (2018)[I]	Taiwan	14	SEC	8.6 ± 3.4	53.9 ± 12.7	14.3	9.0 ± 3.9	/	"Improvement in PASI": 77.7 ± 18.5	/		48.4 ± 50.1	"no significant differences"	/	"no significant differences"	IFN/RIB[1] (4/14) DAA[2] (1/14)	1	HCC
Siegel, S. A. R. et al. (2017)[II]	USA	3	SEC	/	54-64	/	/	/		"no evidence of significant elevations"			/			/	0	/
UST																		
Chiu, H.Y. et al. (2013)[II]	Taiwan	4	UST	8±2.6	64.8±12.1	0	9.5*	/	0/4	"slightly increased" (3/4)			/	"increased" (3/4)		none	1	HCC (1/4)
Siegel, S. A. R. et al. (2019)[II]	USA	11	UST	/	54.3±5.8	27.3	/	BSA 36.5±20.3	BSA 10.8±9.6	/	/	/	no significant elevation** 11/11	7/11 / = 4/11	no significant increase** / = 3/11	3/11[2]	1***	/
> than one treatment																		
Morisco, F. et al. (2014)[II]	Italy	15	ADA, ETA, UST, IFX	/	62±11.8	20	48	/		/	/	25	"unchanged"	/	"unchanged"	none	0	/

Al Mutairi, N. and Abouzaid, H.A. (2018)[I]	Kuwait	7	ADA (7) ETA (1)	13.7±10.4 20	54±12.9	40	41.4±21.4	/	7/7	22 (17–25.8)	21 (17.1–26.4)	23 (12.3–28.8)	23 (14.7–25.3)	"detectable level" (2/4)	"detectable level" (2/4)	/	0	none
Prignano, F. et al. (2011)[II]	Italy	5	ADA (2) ETA (3)	6 8.6	50.4*	25	7.3	/		"unchanged"				"unchanged"		none	0	/
Navarro, R. et al. (2013)[II]	Spain	5	ADA (3) ETA (5) UST (1) IFX (1)	6.7±3.8 15.6±16.2 17 8	39.8±11.3	0	/	14.6±8.3	2/5	110±78.9	145±114.7	106.6±68.1	107.9±46.1	2/5	↓ 1/2 (0) ↑ 1/2 (1.57)	none	0	none
Snast, I. et al. (2017)[II]	Israel	1	ETA ADA	36	78	0	22.3*	BSA 50	1/1	68	32	74	32	/		none	0	none
Chularojanamontri, L. et al. (2021)[II]	Thailand	3	Acitretin (3) CsA (2) ETA (1) IFX (1) MTX (1)	/	52.7±6.4	33.3	/	/	/	46.6±27,8	27±21.7	43±30.6	14.7±4.9	1/3 / = 2/3	/	pegIFN/RIB[2] 1/3 / = 2/3	no worsening of HCV infection during psoriasis treatment'	/

Abbreviation:
/ = data not applicable or reported
1 = before treatment; 2 = while treatment; 3 = no diffrence in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospectice study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; DAA = Direct acting antivirals; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; EFA = Efavirenz; GOL = Golimumab; HCC = Hepatocellular Carcinoma; HCV = Hepatitis C Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; TEN = Tenofovir; PASI = Psoriasis Area Severity Index; PegIFN = Pegylated Interferon; RIB = Ribavirin; SAE = Severe Adverse Event; SEC = Secukinumab; UST = Ustekinumab

Appendix

Table 13: Search strategy for the review update on psoriasis and viral hepatitis (Embase via Ovid)

1	exp psoriasis/ or psoria*.mp.
2	pustulosis palmaris et plantaris.ti,ab.
3	(pustulosis and palm and soles).ti,ab.
4	palmoplantar* pustulosis.ti,ab.
5	1 or 2 or 3 or 4
6	urea/ or urea*.mp.
7	uric acid.mp. or uric acid/
8	salicyl* acid.mp. or salicylic acid/
9	calcineu* inhibito*.mp. or calcineurin inhibitors/
10	tacrolimus/ or pimecrolim*.mp.
11	dithranol*.mp. or anthralin/
12	cortisone/ or cortiso*.mp.
13	betamethasone/ or betametha*.mp.
14	mometaso*.mp. or glucocorticoids/ or mometasone furoate/
15	retinoids/ or tazarot*.mp.
16	coal tar.mp. or coal tar/
17	vit d3.mp or cholecalciferol/
18	calcipotrio*.mp.
19	tacalcito*.mp.
20	calcitriol/ or calcitrio*.mp.
21	phototherap*.mp. or exp phototherapy/
22	puva therapy/ or photochemotherapy/ or puva.mp.
23	exp ultraviolet therapy/ or uv-b therap*.mp.
24	photodynamic therap*.mp.
25	photochemotherap*.mp.
26	light therap*.mp.
27	photoradiation therap*.mp.
28	bbuvb.mp.
29	nbuvb.mp.
30	bb-uvb.mp.
31	nb-uvb.mp.
32	broad band uvb.mp.
33	broad band ultraviolet.mp.
34	narrow band uvb.mp.
35	narrow band ultraviolet.mp.
36	psoralen ultraviolet a.mp.
37	psoralen uva.mp.
38	laser therap*.mp. or laser therapy/
39	ciclospori*.mp. or cyclosporine/
40	cyclospor*.mp.
41	fumar*.mp. or exp fumarates/
42	fumaderm.mp.
43	dimethylfumara*.mp.
44	fae.ti,ab.
45	dmf.ti,ab.
46	exp methotrexate/ or mtx.mp.

47	methotrexa*.mp.
48	amethopterin.mp.
49	mexate.mp.
50	acitretin.mp. or acitretin/
51	retinoids/
52	phosphodiesterase 4 inhibitors/ or apremilast.mp.
53	(etanercep* or enbrel).mp. or etanercept/
54	(infliximab* or remicade).mp. or infliximab/
55	ustekinumab.mp. or ustekinumab/
56	cnto 1275.mp.
57	stelara.mp.
58	secukinumab.mp.
59	guselkumab.mp.
60	adalimumab*.mp. or adalimumab/
61	(d2e7 or humira).mp.
62	exp antibodies, monoclonal/
63	monoclonal antibod*.mp.
64	exp interleukin-23/ or exp interleukin-12/
65	brodalumab.mp.
66	ixekizumab.mp.
67	risankizumab.mp.
68	tildrakizumab.mp.
69	certolizumab.mp.
70	bimekizumab.mp.
71	(tumor necrosis factor-alpha or tumour necrosis factor-alpha).mp.
72	anti tnf.mp.
73	(tumor necrosis factor antibod* or tumour necrosis factor antibod*).mp.
74	(antitumor necrosis factor or antitumour necrosis factor).mp.
75	(anti tumor necrosis factor or anti tumour necrosis factor).mp.
76	(tnf antibod* or tnf alpha antibod*).mp.
77	climate therap*.mp. or climatotherapy/
78	psychotherapy/ or psychosocial therap*.mp.
79	exp tumor necrosis factor-alpha/
80	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79
81	5 and 80
82	exp hepatitis/ or hepatit*.mp.
83	chronic hepatit*.mp. or exp hepatitis, chronic/
84	hepatitis b/ or hepatit* b.mp.
85	hbv.ti,ab.
86	hepatitis c, chronic/ or hepatitis c/ or hepatit* c.mp.
87	non a non b hepatit*.mp.
88	hcv.ti,ab.
89	hepati* d.mp.
90	hepatitis a/ or hepatit* infection.mp.
91	hav.ti,ab.
92	82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91

93	81 and 92

Additional time filters:
("2019*" or "2020*" or "2021*").dc. (Embase)
("2019*" or "2020*" or "2021*").dt. (Medline)

Table 14: Excluded full-texts for the review update on psoriasis and viral hepatitis

A. Abdelmaksoud	2019	study design
V. Brazzelli	2020	study design
L. Cacciola	2020	off-topic
L. Chularojanamontri	2019	double
J. R. Duncan	2019	study design
M. Etminan	2019	off-topic
A. G. A. Farag	2019	off-topic
K. W. Hagberg	2020	off-topic
G. Krishnamoorthy	2019	study design
C. Lasagni	2018	study design
C. S. Lau	2021	off-topic
S. J. Lee	2020	off-topic
M. Llamas-Velasco	2015	off-topic
M. Y. Marzhokhova	2019	russian
A. Narcisi	2020	double
S. Ozcelik	2020	off-topic
S. Piaserico	2019	study design
S. Piaserico	2019	double
I. Raposo	2019	off-topic
S. Sayar	2020	off-topic
G. Schmajuk	2020	off-topic

Original Version

Inclusion criteria

We included all studies on adult patients with a clinical diagnosis of psoriasis and a concomitant hepatitis B or C being treated for psoriasis. Viral hepatitis was defined as positive serological or virological marker for hepatitis B virus (HBV) or hepatitis C virus (HCV) before onset of the psoriasis treatment.

The interventions were specified to be topical treatment (urea, salicylic acid, calcineurin-inhibitors (pimecrolimus, tacrolimus), dithranol, corticosteroids (betamethasone, mometasonfuroat), tazaroten, coal tar, vitamin D3 derivate (calcipotriol, tacalcitol, calcitriol, calcipotriol and betamethasone) or systemic treatment (acitretin, ciclosporin, fumarates, methotrexate, apremilast) for psoriasis including biologicals (TNFi: etanercept, infliximab, adalimumab; Anti-IL12/23: ustekinumab; Anti-IL17: secukinumab, ixekizumab, brodalumab; Anti-IL23). We included studies comparing the intervention to placebo or another treatment and those without comparator.

The following outcomes were of interest:

1. Change in skin lesions based on PASI (Psoriasis Area Severity Index) or PGA (Physician Global Assessment) or another study specific assessment.
2. Transaminases, viral load or other study specific outcomes
3. Type and proportion of other adverse events
4. Quality of life based on SF-36 (The Short Form (36) Health Survey), DLQI (Dermatology Life Quality Index) or another study specific assessment.

When possible, we evaluated the outcomes at different timings, based on what was reported in the publications (e.g. short-term, long-term).

Included were randomized controlled trials, clinical trials (with and without comparison group), cohort studies, case control studies and cross sectional studies. We used a step-wise approach for including studies (for each study drug and comparator) following the hierarchy of evidence (Murad et al., 2016).

We excluded studies on patients with psoriatic arthritis because of the different pathophysiology and treatment options.

Information sources

Three databases were searched systematically (MEDLINE Ovid from 1946, Embase Ovid from 1974 and

The Cochrane Central Register of Controlled Trials (CENTRAL); updated last in January 2019).

Furthermore, we examined the reference lists of included studies to identify references to relevant

trials. The full search strategy is shown below.

Data collection, statistical analysis and evaluation

We screened all identified abstracts/titles for eligibility. Included titles/abstracts were then screened

as full texts based on the above listed eligibility criteria.

Endnote was used to manage all records. One reviewer performed the screening and did the data extraction using a standardized form. A second reviewer checked 50% of the data with high agreement. We recorded all full-texts excluded and the primary reason for exclusion (see below).

The following items were extracted: Author, year of publication, country in which the study took place, study design, inclusion and exclusion criteria, baseline characteristics of the included patients, details of the interventions, details of any co-interventions, number and reasons for drop-out, type of adverse events and proportion of patients experiencing adverse events and serious adverse events, proportion of patients who experienced worsening of liver function, proportion of patients who showed an improvement in skin lesions, proportion of patients who showed an improvement in quality of life, time of assessment of endpoints and number/rate of patients assessed.

Risk of bias assessment

We assigned Levels of Evidence for all studies included using the Center of Evidence Based Medicine Oxford recommendations (OCEBM Levels of Evidence Working Group) [3]. To assess risk of bias in randomized trials we additionally used the RoB 2.0 tool [4]. We planned to use the ROBINS-I tool for controlled, non-randomized studies of interventions but none of these study types were included[37].

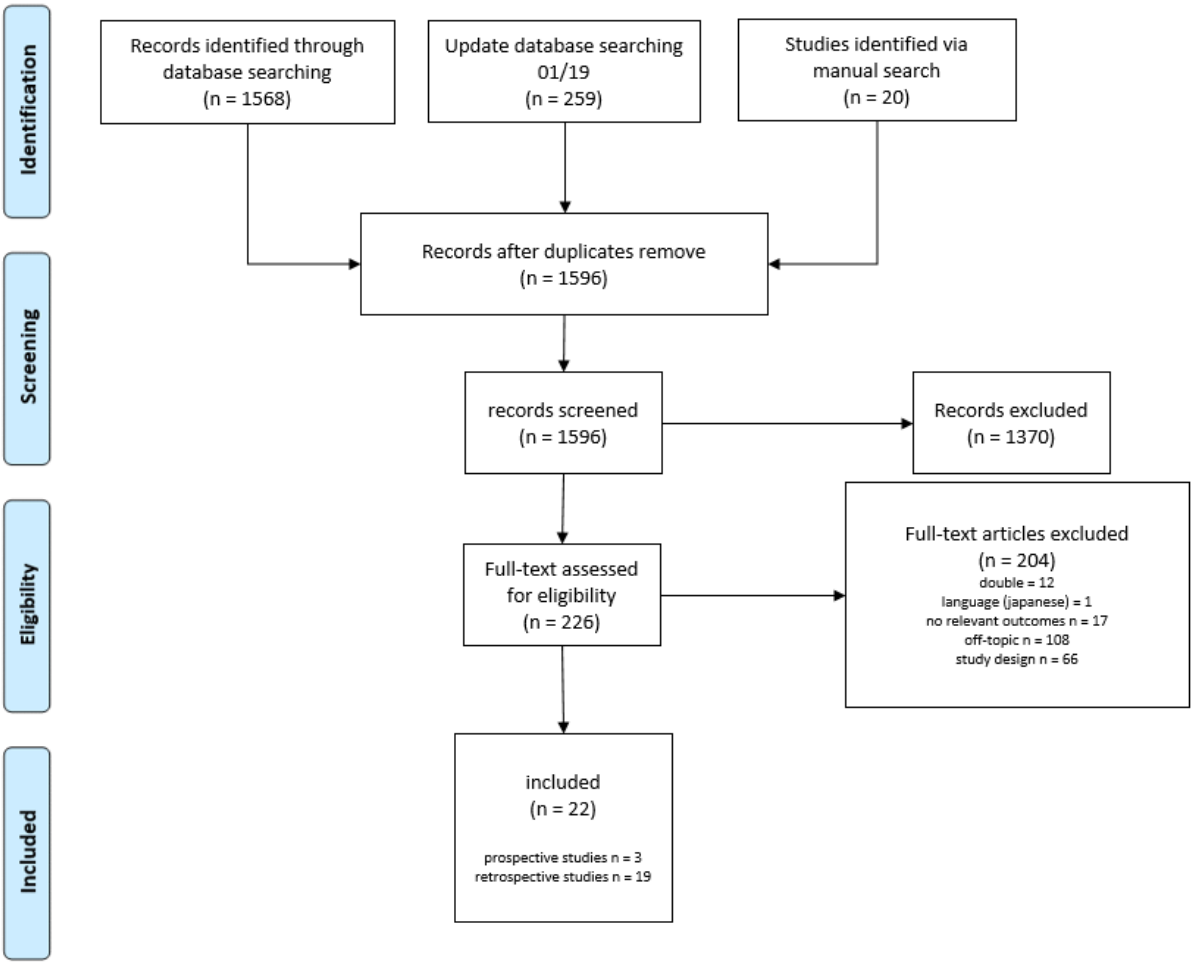
Data were summarized and sorted by the medication used (see Table 16 and Table 17). We counted the number of patients across studies reported to have liver dysfunction or HBV/HCV-reactivation during follow-up and improvement in psoriasis to provide a pragmatic overview. We summarized the results with focus on clinically relevant information (e.g. liver dysfunction or HBV/HCV-reactivation).

Results

Our search yielded 1596 citations, 22 of which fulfilled the inclusion criteria (January 2019; see study selection flow chart). Three prospective studies [5-7], two studies based on registry data [1,8] and 17 retrospective studies [9-25] were included.

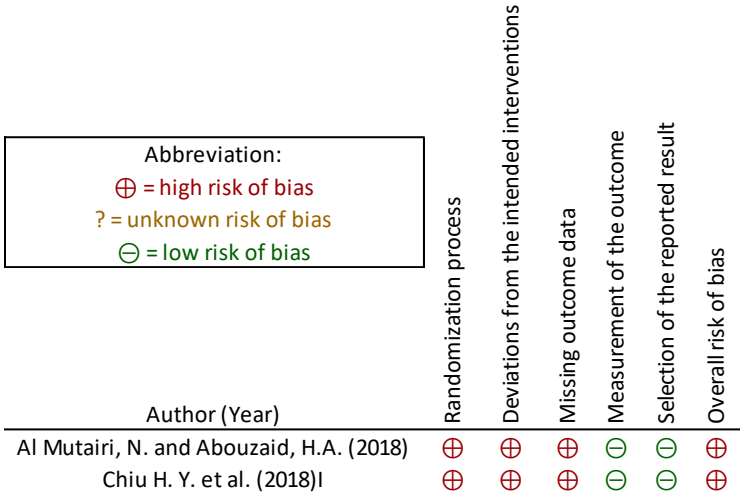
No studies on acitretin, apremilast, brodalumab, ciclosporin, fumarates, guselkumab, ixekizumab, risankizumab and tildrakizumab were identified that reported outcomes for viral hepatitis.

Figure 4: Study selection flowchart for the selection of studies for the review update on psoriasis and viral hepatitis



Based on the Center of Evidence Based Medicine Oxford recommendations all references included were rated level 3 (Ting et al., 2018, Chiu et al., 2018, AlMutairi and Abouzaid, 2018, Cho et al., 2012, Nosotti et al., 2010, Cassano et al., 2011, Hsieh et al., 2018, Pereira et al., 2018, Siegel et al., 2017, Piaserico et al., 2017a, Chiu et al., 2013, Fotiadou et al., 2011, Garavaglia and Altomare, 2010, Morisco et al., 2014, Navarro et al., 2013, Piaserico et al., 2017b, Snast et al., 2017, Navarro et al., 2014, Prignano et al., 2011, Di Nuzzo et al., 2013, Sanz-Bueno et al., 2015, Tang et al., 2018, OCEBM Levels of Evidence Working Group and * OCEBM Levels of Evidence Working Group = Jeremy Howick, 2011). Results of the additional assignment for prospective randomized studies are shown in Table 15 (Chiu et al., 2018, AlMutairi and Abouzaid, 2018, Higgins JPT, 2016).

Table 15: Risk of bias in prospective studies



RISK OF BIAS – PROSPECTIVE RANDOMIZED STUDIES

Data for overall 1128 patients with psoriasis and viral hepatitis was extracted. Of those, 854 patients suffered from hepatitis B infection and 274 from hepatitis C infection. Most of the included studies reported individual patient data. The tables below are providing detailed information, sorted by medication used.

Table 16: Hepatitis B

Hepatitis B

								Severity score (e.g. PASI)		Transaminases				Viral load >2000 IU/ml				
										AST mean±SD		ALT mean±SD						
Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Baseline mean±SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Base-line (n)	Eof (n)	Antiviral therapy	HBV reactivation (n)[4]	Other adverse events
		ADA																
Piaserico, S et al. (2017)[II]	Italy	17	ADA	27*	50.8±12.5	35.3	/	21.2±6.9	16/17	39±25.4	40.4±25	39.7±27.8	44.9±30.4	0	0	LAM[1] (8/17) LAM/ENT[1] (1/17)	0	/
Fotiadou, C. et al. (2011)[II]	Greece	3	ADA	12±3	53.7± 10.6	33.3	6-24	14.1±2	3/3	19.3±2.1	20.7±1.2	21±2.6	21.3±2.5	0	0	none	0	/
Nosotti, L. et al. (2010)[II]	Italy	3	ADA	9.1±3.7	54±7.2	33.3	/	12.1±13.7	/	13±1.7	18.7±4.2	unchanged	unchanged	0	0	none	0	/
Navarro, R. et al. (2014)[II]	Spain	2	ADA	11 26	74 68	50	/	/		17 9	19 21	20 14	20 43	/		none	0	/
Snast, I. et al. (2017)[II]	Israel	2	ADA	12 72	55 69	0	63.7*	26.1 BSA 50	2/2 PASI50	35 19	29 34	34 24	42 14	0	0	none	0	Pneumonia (1/2)
Cho, Y.T. et al. (2012)[II]	Taiwan	1	ADA	27	44	0	14	/		15	46	22	34	0	0	none	0	none
		ETA																
Prignano, F. et al. (2011)[II]	Italy	11	ETA	8.6*	61.4*	27.3	7.3	/		unchanged				0	0	none	0	/
Snast, I. et al. (2017)[II]	Israel	8	ETA	55.2±46.3	57.3±12.2	37.5	63.7*	19.8±2.7 BSA 50 (4/8)	8/8 PASI50	27.6±16.8	22.2±7.2	24±9.2	19.5±8.5	0	0	LAM[2] (1/8)	0	none
Navarro, R. et al. (2014)[II]	Spain	7	ETA	28.7±20.7	60.6±15.4	28.6	/	/		34.9±14.9	34.7±21.4	44±23.4	32.6±19.6	/		none	0	/
Cho, Y.T. et al. (2012)[II]	Taiwan	6	ETA	24.8±12.7	42.6±4.1	16.7	31.3±13	/		34.5±26.7	35.5±8.2	33.3±24.6	47±28.9	2	2	LAM[2] (1/6) LAM/ENT[2] (1/6)	3/6	none
Nosotti, L. et al. (2010)[II]	Italy	4	ETA	10.5±5.7	51.3±5.7	0	/	7.4±4.6	/	23.5±3.1	28.3±5.7	unchanged	unchanged	0	0	LAM[2] (1/4)	0	/
Fotiadou, C. et al. (2011)[II]	Greece	3	ETA	12.1±5.9	49.7±14	66.7	6-24	12.1±2.2	3/3	17.3±1.5	18.3±1.5	20.3±3.1	22.7±3.2	0	0	LAM[2] (1/3)	0	/
Navarro, R. et al. (2013)[II]	Spain	3	ETA	27±19	43.7±13	33.3	25*	19.7±4.8	2/3 PASI50	28.3±4	44.3±14.6	46.3±3	45.7±13.7	1	0	ADE/ENT[2] (1/3) LAM[2] (2/3)	0	none

Abbreviation:
1 = before treatment; 2 = while treatment; 3 = no difference in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospective study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab;
HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; SEC = Secukinumab; UST = Ustekinumab

Hepatitis B

Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Severity score (e.g. PASI)		Transaminases				Viral load >2000 IU/ml		Antiviral therapy	HBV reactivation (n)[4]	Other adverse events
										AST mean±SD		ALT mean±SD						
								Baseline mean±SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Base-line (n)	Eof (n)			
		IFX																
Navarro, R. et al. (2014)[II]	Spain	4	IFX	25.5±10.3	60.5±10	25	/		/	28.5±8.3	30.8±15.2	30.3±14.8	19.8±8.7		/	none	0	/
Fotiadou, C. et al. (2011)[II]	Greece	1	IFX	10	48	100	6-24	20.2	1/1	25	30	31	40	0	0	none	0	/
Navarro, R. et al. (2013)[II]	Spain	1	IFX	37	36	100	25*	22.2	0	42	52	64	62	0	0	LAM[2]	0	none
		MTX																
Tang, K. T. et al. (2018)[II]	Taiwan	370	MTX	/	42.6±13.2	28	50.4 ±38.4		/			/			/	48/370	/	Liver cirrhosis (15/370)[3]
		SEC																
Chiu H. Y. et al. (2018)[I]	Taiwan	25	SEC	7.7 ± 3.8	49.7 ± 8.6	16	9.1 ± 3.9	13.4 ± 8.2	/		/	43.7±42.2	/		/	3/25[1]	6/25	Hepatic cancer
		24		8.7 ± 3.7	54.7 ± 13.4	25	9.2 ± 3.7	20.1 ± 8.3				41.1 ± 28.0				11/24[1]	1/24	/
		UST																
Ting, S. W. et al. (2018)[I]	Taiwan	54	UST	/	47*	16.7	24*		/			"none had liver failure"				ENT[1] (1/54) LAM[2] (1/54)	3/48	/
Hsieh, T. Y. et al. (2018)[II]	Taiwan	75	UST	/	/	/	24.7*		/			/			/	unknown[2] (2/75)	2/75	/
Chiu, H.Y. et al. (2013)[II]	Taiwan	14	UST	9.4±9	45.5±7.6	28.6	10.4*	/	5/14			unchanged		/	"increased" (4/14)	ENT[2] (4/14)	2/14	/
Piaserico, S. et al. (2017)	Italien	5	UST	57.2±13.9	55.4±16.5	20	57		/	28.8±11.6	31.8±7.9	31.2±16.2	41.8±19	0	0	LAM[1] (4/5)	0	/
Navarro, R. et al. (2013)[II]	Spain	1	UST	7	56	0	25*	17.6	1/1 PASI50	32	16	35	15	1/1	0	ENT[2]	0	none

Abbreviation:
1 = before treatment; 2 = while treatment; 3 = no difference in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospective study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab;
HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; SEC = Secukinumab; UST = Ustekinumab

Hepatitis B

Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Severity score (e.g. PASI)		Transaminases				Viral load >2000 IU/ml		Antiviral therapy	HBV reactivation (n)[4]	Other adverse events
										AST mean±SD		ALT mean±SD						
								Baseline mean±SD	e.g. PASI-75 response eof (n)	Baseline	Eof	Baseline	Eof	Base-line (n)	Eof (n)			
		IFX																
Navarro, R. et al. (2014)[II]	Spain	4	IFX	25.5±10.3	60.5±10	25	/		/	28.5±8.3	30.8±15.2	30.3±14.8	19.8±8.7		/	none	0	/
Fotiadou, C. et al. (2011)[II]	Greece	1	IFX	10	48	100	6-24	20.2	1/1	25	30	31	40	0	0	none	0	/
Navarro, R. et al. (2013)[II]	Spain	1	IFX	37	36	100	25*	22.2	0	42	52	64	62	0	0	LAM[2]	0	none
		MTX																
Tang, K. T. et al. (2018)[II]	Taiwan	370	MTX	/	42.6±13.2	28	50.4 ±38.4		/			/			/	48/370	/	Liver cirrhosis (15/370)[3]
		SEC																
Chiu H. Y. et al. (2018)[I]	Taiwan	25	SEC	7.7 ± 3.8	49.7 ± 8.6	16	9.1 ± 3.9	13.4 ± 8.2	/		/	43.7±42.2	/		/	3/25[1]	6/25	Hepatic cancer
		24		8.7 ± 3.7	54.7 ± 13.4	25	9.2 ± 3.7	20.1 ± 8.3				41.1 ± 28.0				11/24[1]	1/24	/
		UST																
Ting, S. W. et al. (2018)[I]	Taiwan	54	UST	/	47*	16.7	24*		/			"none had liver failure"				ENT[1] (1/54) LAM[2] (1/54)	3/48	/
Hsieh, T. Y. et al. (2018)[II]	Taiwan	75	UST	/	/	/	24.7*		/			/			/	unknown[2] (2/75)	2/75	/
Chiu, H.Y. et al. (2013)[II]	Taiwan	14	UST	9.4±9	45.5±7.6	28.6	10.4*	/	5/14			unchanged		/	"increased" (4/14)	ENT[2] (4/14)	2/14	/
Piaserico, S. et al. (2017)	Italien	5	UST	57.2±13.9	55.4±16.5	20	57		/	28.8±11.6	31.8±7.9	31.2±16.2	41.8±19	0	0	LAM[1] (4/5)	0	/
Navarro, R. et al. (2013)[II]	Spain	1	UST	7	56	0	25*	17.6	1/1 PASI50	32	16	35	15	1/1	0	ENT[2]	0	none

Abbreviation:
1 = before treatment; 2 = while treatment; 3 = no difference in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospective study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab;
HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; SEC = Secukinumab; UST = Ustekinumab

Hepatitis B

Author (Y)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Eof (M) mean±SD	Severity score (e.g. PASI)		Transaminases				Viral load >2000 IU/ml		Antiviral therapy	HBV reactivation (n)[4]	Other adverse events
								Baseline mean±SD	e.g. PASI-75 response eof (n)	AST mean±SD		ALT mean±SD		Base-line (n)	Eof (n)			
										Baseline	Eof	Baseline	Eof					
		> than one treatment																
Cassano N. et al. (2010)[II]	Italy	62	ETA (44) ADA (10) IFX (8)	27.8* 19* 28.8*	54*	32.3	55	15.3 (10.2-39.9)	/		"normal value"			"undetectable"		LAM[2] (1/62)	0	/
Morisco, F. et al. (2014)[II]	Italy	23 36	ADA, ETA, UST, IFX, MTX, CsA	/	66±10.6 52±12.4	56.5 25	/	/		/	unchanged	27±2.3 24±3.2	unchanged	0	0	none	0	/
Al Mutairi, N. and Abouzaid, H.A. (2018)[I]	Kuwait	28 4	ADA (11) ETA (10) UST (8) ADA (3) ETA (4) UST (1)	14.7±12.3 21.7±25.3 30±14.7 15.4±11.7 18.5±23.6 28±11.9	51±13.2 49±15.6	10.7 25	41.4 ±21.4	14.2±1.5	28/28 4/4	22 (17–25.8)	23 (12.3–28.8)	21 (17.1–26.4)	23 (14.7–25.3)	0		none LAM[2] (4/4)	0	none
Pereira, R.et al. (2018)[II]	Portugal	26	ETA (12) ADA (8) IFX (6) >1 (13)	37.2 50.4 58.8 /	52.7±14.1	38.5	43.6 ±28.7	/		/				"undetectable"		/	0	/
Sanz-Bueno, J. (2015)[I]	Spain	20	ADA (13) ETA (7) UST (6) IFX (7)	13 16 18 22	/	25	40*	/		unchanged				0	0	none	0	/
Snast, I. et al. (2017)[II]	Israel	16	ETA (16), ADA (14), IFX (5), UST (12), SEC (3), GOL (1), ALE (1)	70.8±32.4	55.2±11.4	31.3	63.7*	23.3±8.6 BSA 50 (5/16) BSA 70 (1/16)	9/16 PASI50	22.7±5.6	21.9±8.3	21.5±7	19.3±10.7	0	0	LAM[2] (1/16)	0	Respiratory infection (1/16), myocardial infarction (1/16) erythema (2/16)

Abbreviation:
1 = before treatment; 2 = while treatment; 3 = no difference in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospective study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ADE = Adefovir; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; CsA = Cyclosporine A; ENT = Entecavir; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab;
HCC = Hepatocellular Carcinoma; HBV = Hepatitis B Virus; IFN = Interferon; IFX = Infliximab; LAM = Lamivudine; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; SEC = Secukinumab; UST = Ustekinumab

Table 17: Hepatitis C

Hepatitis C

										Transaminases							
								Severity Score (e.g. PASI)		AST mean±SD		ALT mean±SD		Viral load			
Author (Year)	Place	Patients (n)	Drug	Duration of treatment (M) mean±SD	Age (Y) mean±SD	♀ (%)	Duration of follow-up (M) mean±SD	Baseline mean±SD	e.g. PASI-75 response, eof (n)	Baseline	Eof	Baseline	Eof	Baseline detectable (n)	Change at eof (q)	Antiviral therapy (n)	HCV reactivation (n)	Adverse envent
		ADA																
Piaserico, S et al. (2017)[II]	Italy	20	ADA	40*	49.8±11.3	30	/	15.8±6.2	14/20	39.5±21.2	53.9±32.7	38±20.7	57.3±36.4	16/20	↓ 7/16 (0.7±0.3) ↑ 9/16 (8.8±17.1)	RIB[1] (1/20) IFN/RIB[1] (1/20)	0	/
Navarro, R. et al. (2013)[II]	Spain	1	ADA	2	65	0	/	15.6	0/1	20	30	34	55	1/1	↑ (1.03)	none	0	Stroke (1/1)
		ETA																
Navarro, R. et al. (2013)[II]	Spain	12	ETA	15.5±5.9	51.5±12.8	16.7	/	17.8±8.8	6/12	82.8±42.2	61.9±31	88.1±40.9	53.1±22.5	6/12	↓ 4/6 (0.04±0.08) ↑ 2/6 (8.2±12)	IFN/RIB[2] (3/12)	0	Respiratory Infection (1/12) HCC (2/12)
Garavaglia, M.C. et al. (2010)[II]	Italy	5	ETA	15.6±7.1	59±10.7	20	7-24	22.9±3.2	4/5	42.8±14.1	43±23.6	49±10.5	52.4±37.7	4/5	↓ 3/4 (0.64±0.5) ↑ 1/4 (1.22)	IFN/RIB[2] (1/5)	0	/
Di Nuzzo, S. et al. (2013)[II]	Italy	5	ETA	12*	60*	0	/		/	"increased" (2/5)				"unchanged"		/	0	HCC (1/5)
Snast, I. et al. (2017)[II]	Israel	3	ETA	18±9.6	57±16.6	0	22.3 (8-36)	19.5±6.7	2/3	48.3±7.6	53.7±18.6	58.7±5.7	72.3±22.9	3/3	↓ 1/3 (0) ↑ 2/3 (1.93±0.93)	none	0	none
		MTX																
Tang, K. T. et al. (2018)[II]	Taiwan	174	MTX	/	50.4±12.6	36	57.6±42		/			/			/	42/174	/	Liver cirrhosis (19/174)[3]
		SEC																
Chiu, H. Y. et al. (2018)[I]	Taiwan	14	SEC	8.6 ± 3.4	53.9 ± 12.7	14.3	9.0 ± 3.9	/	"Improvement in PASI": 77.7 ± 18.5	/		48.4 ± 50.1	"no significant differences"	/	"no significant differences"	IFN/RIB[1] (4/14) DAA[2] (1/14)	1	HCC
Siegel, S. A. R. et al. (2017)[II]	USA	3	SEC	/	54-64	/	/		/	"no evidence of significant elevations"					/	/	0	/
		UST																
Chiu, H.Y. et al. (2013)[II]	Taiwan	4	UST	8±2.6	64.8±12.1	0	9.5*	/	0/4	"slightly increased" (3/4)				/	"increased" (3/4)	none	1	HCC (1/4)
		more than one treatment (n)																
Morisco, F. et al. (2014)[II]	Italy	15	ADA, ETA, UST, IFX	/	62±11.8	20	48		/	/	/	25	"unchanged"	/	"unchanged"	none	0	/
Al Mutairi, N. and Abouzaid, H.A. (2018)[I]	Kuwait	7	ADA (7) ETA (1)	13.7±10.4 20	54±12.9	40	41.4±21.4	/	7/7	22 (17–25.8)	21 (17.1–26.4)	23 (12.3–28.8)	23 (14.7–25.3)	"detectable level" (2/4)	"detectable level" (2/4)	/	0	none
Prignano, F. et al. (2011)[II]	Italy	5	ADA (2) ETA (3)	6 8.6	50.4*	25	7.3		/	"unchanged"				"unchanged"		none	0	/
Navarro, R. et al. (2013)[II]	Spain	5	ADA (3) ETA (5) UST (1) IFX (1)	6.7±3.8 15.6±16.2 17 8	39.8±11.3	0	/	14.6±8.3	2/5	110±78.9	145±114.7	106.6±68.1	107.9±46.1	2/5	↓ 1/2 (0) ↑ 1/2 (1.57)	none	0	none
Snast, I. et al. (2017)[II]	Israel	1	ETA ADA	36	78	0	22.3*	BSA 50	1/1	68	32	74	32		/	none	0	none

Abbreviation:
1 = before treatment; 2 = while treatment; 3 = no difference in the occurrence of liver cirrhosis between MTX-users and a second cohort without MTX; 4 = as defined in the study at end of follow
I = prospective study; II = retrospective study
* = mean (SD not applicable or reported); ** = as defined by threefold increase in transaminases or 10-fold increase in viral load; *** = HCV-reactivation 6 month prior antiviral therapy reported
ADA = Adalimumab; ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BSA = Body Surface Area; DAA = Direct acting antivirals; ETA = Etanercept; eof = end of follow-up; GOL = Golimumab; HCC = Hepatocellular Carcinoma; HCV = Hepatitis C Virus;
IFN = Interferon; IFX = Infliximab; MTX = Methotrexate; PASI = Psoriasis Area Severity Index; RIB = Ribavirin; SEC = Secukinumab; UST = Ustekinumab

Table 18: Search strategy for the review on psoriasis and viral hepatitis (Embase Ovid)

1. exp Psoriasis/ or Psoria*.mp.
2. pustulosis palmaris et plantaris.ti,ab.
3. (pustulosis and palm and soles).ti,ab.
4. palmoplantar* pustulosis.ti,ab.
5. 1 or 2 or 3 or 4
6. Urea/ or Urea*.mp.
7. uric acid.mp. or Uric Acid/
8. salicyl* acid.mp. or Salicylic Acid/
9. Calcineu* inhibito*.mp. or Calcineurin Inhibitors/
10. Tacrolimus/ or Pimecrolim*.mp.
11. dithranol*.mp. or Anthralin/
12. Cortisone/ or cortiso*.mp.
13. Betamethasone/ or Betametha*.mp.
14. mometaso*.mp. or Glucocorticoids/ or Mometasone Furoate/
15. Retinoids/ or tazarot*.mp.
16. coal tar.mp. or Coal Tar/ 17. vit d3.mp or Cholecalciferol/
18. calcipotrio*.mp.
19. tacalcito*.mp.
20. Calcitriol/ or calcitrio*.mp.
21. phototherap*.mp. or exp Phototherapy/
22. PUVA Therapy/ or Photochemotherapy/ or PUVA.mp.
23. exp Ultraviolet Therapy/ or UV-B therap*.mp.
24. photodynamic therap*.mp.
25. photochemotherap*.mp.
26. light therap*.mp.
27. photoradiation therap*.mp.
28. BBUVB.mp.
29. NBUVB.mp.
30. BB-UVB.mp.
31. NB-UVB.mp.
32. broad band uvb.mp.
33. broad band ultraviolet.mp.
34. narrow band uvb.mp.
35. narrow band ultraviolet.mp.

36. psoralen ultraviolet a.mp.
37. psoralen uva.mp.
38. Laser therap*.mp. or Laser Therapy/
39. Ciclospori*.mp. or Cyclosporine/
40. cyclospor*.mp.
41. fumar*.mp. or exp Fumarates/
42. fumaderm.mp.
43. dimethylfumara*.mp.
44. fae.ti,ab.
45. dmf.ti,ab.
46. exp Methotrexate/ or MTX.mp.
47. methotrexa*.mp.
48. amethopterin.mp.
49. mexate.mp.
50. acitretin.mp. or Acitretin/
51. Retinoids/
52. Phosphodiesterase 4 Inhibitors/ or apremilast.mp.
53. cdp571.mp.
54. (etanercep* or enbrel).mp. or Etanercept/
55. (Infliximab* or remicade).mp. or Infliximab/
56. ustekinumab.mp. or Ustekinumab/
57. (briakinumab or ABT-874).mp.
58. CNTO 1275.mp.
59. stelara.mp.
60. secukinumab.mp.
61. guselkumab.mp.
62. adalimumab*.mp. or Adalimumab/
63. (d2e7 or humira).mp.
64. exp Antibodies, Monoclonal/
65. monoclonal antibod*.mp.
66. exp Interleukin-23/ or exp Interleukin-12/
67. brodalumab.mp.
68. ixekizumab.mp.
69. (tumor necrosis factor-alpha or tumour necrosis factor-alpha).mp.
70. anti tnf.mp.

71. (tumor necrosis factor antibod* or tumour necrosis factor antibod*).mp.
72. (antitumor necrosis factor or antitumour necrosis factor).mp.
73. (anti tumor necrosis factor or anti tumour necrosis factor).mp.
74. (tnf antibod* or tnf alpha antibod*).mp.
75. climate therap*.mp. or Climatotherapy/
76. Psychotherapy/ or psychosocial therap*.mp.
77. exp Tumor Necrosis Factor-alpha/
78. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77
79. 5 and 78
80. exp Hepatitis/ or Hepatit*.mp.
81. chronic hepatit*.mp. or exp Hepatitis, Chronic/
82. Hepatitis B/ or hepatit* b.mp.
83. HBV.ti,ab.
84. Hepatitis C, Chronic/ or Hepatitis C/ or hepatit* c.mp.
85. non a non b hepatit*.mp.
86. HCV.ti,ab.
87. hepati* d.mp.
88. Hepatitis A/ or hepatit* infection.mp.
89. HAV.ti,ab.
90. 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89
91. 79 and 90

Table 19: Excluded full-texts for the review on psoriasis and viral hepatitis

A. Abuchar	2013	study design
A. J. Alcaide	2008	study design
N. AlMutairi and H. A. Abouzaid	2018	double
Anonymous	2003	off-topic
Anonymous	2016	double
E. A. Antoniou	2016	off-topic
M. Armengot-Carbo	2013	off-topic
S. Ashraf	2013	off-topic
S. Aslanidis	2007	off-topic
G. Babino	2013	study design
F. Bartalesi	2013	study design
S. E. Behnam	2010	study design
G. Berge	1970	off-topic
S. L. Bevans	2018	study design
S. L. Bevans	2018	study design
E. Bjornsson	2015	off-topic

M. J. Boffa	1995	off-topic
L. Bomm	2011	study design
C. Bonifati	2016	study design
W. W. Bottomley	1990	study design
D. E. Branisteanu	2010	no relevant outcomes
V. Brazzelli	2012	off-topic
N. P. Burrows	1995	off-topic
M. V. Cannizzaro	2017	study design
S. C. Carneiro	2008	off-topic
N. Cassano and G. A. Vena	2008	off-topic
I. Cavazzana	2008	off-topic
R. Cecchi and L. Bartoli	2006	study design
P. Cetkovska	2015	off-topic
M. Chima and M. Lebwohl	2018	off-topic
A. Chiricozzi	2018	off-topic
Y. Chiu	2018	no relevant outcomes
Y. M. Chiu	2018	no relevant outcomes
Y. M. Chiu	2017	no relevant outcomes
Y. M. Chiu	2017	off-topic
E. Chouela	1996	off-topic
C. H. Chu and C. Davis	2017	study design
W. T. Clarke	2018	off-topic
M. H. Collazo	2008	study design
A. Conde-Taboada	2009	study design
S. Couderc	2015	off-topic
M. S. Dag	2013	off-topic
B. Dahmani and O. Boudghene Stambouli	2013	off-topic
L. J. Dang	2014	off-topic
C. De Simone	2006	study design
V. Di Lernia and E. Guareschi	2010	off-topic
V. Di Lernia	2013	study design
S. Di Nuzzo	2016	study design
A. M. Downs and M. G. Dunnill	2000	off-topic
H. V. Dubin and E. R. Harrell	1970	off-topic
C. Efe	2010	off-topic
K. Eisendle and P. Fritsch	2005	study design
A. A. Elfert	2017	off-topic
M. Enomoto	2018	off-topic
M. Enomoto	2018	off-topic
E. Erkek	2000	study design
M. Esposito	2017	off-topic
D. A. Fairhurst and R. Sheehan-Dare	2009	off-topic
B. Feaster	2018	study design
D. J. Filip	1971	off-topic
A. Finet	2016	off-topic
B. Foroncewicz	2014	off-topic
C. Fotiadou	2018	study design
M. Galeazzi	2007	study design
R. K. Gandhi	2010	study design
I. Garcia-Doval	2012	off-topic
E. Garcia-Lora	1993	no relevant outcomes
B. Ghang	2017	study design
A. M. Giovanna Brunasso	2012	study design
G. Girolomoni	2012	study design
R. Gish	2018	study design
P. Gisondi	2009	off-topic
C. Goujon	2010	off-topic
F. Heppt and M. Sticherling	2016	no relevant outcomes
F. Heppt and M. Sticherling	2017	off-topic

F. Heppt and M. Sticherling	2017	study design
T. Y. Hsieh	2018	double
S. Imafuku	2007	study design
M. Jablkowski	1997	off-topic
C. Jeon	2017	study design
C. Jeon	2017	study design
W. Jo	2017	off-topic
J. Juan and J. J. Feld	2014	study design
W. Kaabi	2013	study design
T. Kaiser	2009	off-topic
Y. Kano	2006	off-topic
M. Karray	2016	off-topic
E. D. Kartal	2005	no relevant outcomes
S. B. Kaushik and M. G. Lebwohl	2019	study design
S. Kikuchi	2018	double
S. Kikuchi	2018	study design
G. W. Kim	2013	off-topic
L. E. King Jr	1975	off-topic
L. E. King	1975	off-topic
N. Kluger	2009	off-topic
B. Kok	2018	off-topic
M. Kono	2016	language
J. Koskinas	2013	study design
M. Kouba	2012	study design
C. Kreiss	2002	off-topic
J. T. Kuenstner	2015	off-topic
C. Lasagni	2018	study design
R. Laurenti	2013	off-topic
J. A. Leithead	2009	off-topic
E. Lemmenmeier	2016	off-topic
C. Leonardi	2019	off-topic
C. Leonardi	2010	off-topic
Z. X. Li	2012	study design
G. Linardaki	2007	study design
M. Llamas-Velasco	2015	off-topic
M. Llamas-Velasco	2015	off-topic
A. Lonardo	2001	off-topic
R. Lovero	2017	off-topic
C. Luan	2014	study design
M. A. Magliocco and A. B. Gottlieb	2004	study design
N. Maki	2013	off-topic
G. Malara	2012	no relevant outcomes
I. F. Manalo	2015	study design
V. Manfreda	2019	off-topic
R. Manfredi	2010	off-topic
R. Manfredi and S. Sabbatani	2010	off-topic
V. Martinez-Santana	2018	study design
A. Mebazaa	2009	no relevant outcomes
G. H. Millward-Sadler and T. J. Ryan	1974	off-topic
H. Miura	1999	study design
M. Moghoofei	2018	study design
C. C. Mok	2014	off-topic
S. Nakayama	2013	off-topic
R. Nankani	2017	off-topic
D. J. No	2017	double
D. J. No	2017	study design
L. Nosotti	2011	no relevant outcomes
A. Nyfors and H. Poulsen	1977	off-topic
R. Olteanu	2016	no relevant outcomes
R. A. O'Rourke and G. E. Eckert	1964	off-topic

K. A. Papp	2017	off-topic
A. Paradisi	2010	study design
D. M. Pariser and R. J. Wyles	1980	off-topic
M. P. Pauly	2018	no relevant outcomes
F. Peccerillo	2018	study design
Z. Pena	2016	off-topic
L. Pescitelli	2018	study design
S. Piaserico	2017	double
D. Piccolo	2008	study design
G. Pitarch	2007	off-topic
Y. Poulin and G. Therien	2010	off-topic
F. Prestinari	2010	study design
F. Prignano	2011	study design
F. Prignano	2009	off-topic
S. Purnak and T. Purnak	2014	off-topic
R. Rahamimov	1995	off-topic
A. R. Raymundo	2016	study design
S. P. Reddy	2017	study design
K. Reich	2011	off-topic
H. Riad	2013	off-topic
F. Ricceri	2017	double
A. G. Richetta	2009	no relevant outcomes
H. H. Roenigk, Jr.	1999	off-topic
H. H. Roenigk Jr	1971	off-topic
H. H. Roenigk Jr	1971	off-topic
C. Rokhsar	2006	study design
S. Rosner	2014	off-topic
S. Sabbatani and R. Manfredi	2010	off-topic
M. Salvi	2016	study design
M. D. F. Santos Paim De Oliveira	2012	study design
J. Sanz-Bueno	2015	double
R. Saraceno	2007	off-topic
E. C. Schwaneck	2018	no relevant outcomes
S. Siegel	2015	double
C. H. Smith	2017	study design
A. H. Solay	2018	no relevant outcomes
W. Sondermann	2017	off-topic
R. B. Steglich	2014	study design
R. B. Stephens and A. Cooper	1999	off-topic
H. Y. Suh	2017	off-topic
Y. Takagi	2000	study design
H. Talat	2017	off-topic
A. Tamburello	2018	off-topic
C. Taylor	2000	off-topic
N. S. Tekin	2010	study design
S. W. Ting	2018	double
J. C. Titos-Arcos	2011	off-topic
H. Tobias and R. Auerbach	1973	off-topic
E. Tula	2017	off-topic
C. H. Tung	2016	off-topic
S. Tyring	2007	off-topic
T. K. Uzuncakmak	2016	off-topic
D. Van Der Heijde	2018	off-topic
F. Ventura	2010	study design
F. Verhoeven	2018	off-topic
D. G. Vilas	2012	off-topic
G. D. Weinstein	1970	off-topic
V. C. Weiss	1985	off-topic
L. U. Wolfer	1996	off-topic
M. C. Wu and J. Y. Lee	2012	off-topic

T. Yamamoto	2005	no relevant outcomes
T. Yamamoto	2005	no relevant outcomes
S. Yanagihara	2017	double
S. Yanagihara	2017	study design
H. Zachariae	1984	off-topic
H. Zachariae	1988	off-topic
M. Zanni	2011	study design
M. Zarei	2016	double
N. N. Zein	2005	off-topic

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