RA treatment in special situation

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2020

RA treatment and Hepatic Diseases

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Table 2.

Guidelines on screening for hepatitis B virus markers before immunosuppression or chemotherapy

Society	Who should be screened?	Screening tests
AGA	Patients at moderate or high risk of HBVr	HBsAg, anti-HBc + HBV DNA in case of positive results
ASCO	Groups at heightened risk for chronic HBV infection or if highly immunosuppressive treatment is planned	HBsAg+- anti-HBc in some populations
CDC	All persons receiving cytotoxic or immunosuppressive therapy	HBsAg, anti-HBc, and anti-HBs
DGHO	Groups at heightened risk	HBsAg, anti-HBc + HBV DNA in case of positive results
ECCO	All IBD patients at diagnosis	HBsAg, anti-HBc, and anti-HBs + HBV DNA in case of positive results
EASL	All candidates for chemotherapy and immunosuppression	HBsAg, anti-HBc, and anti-HBs +HBV DNA in case of positive results

AGA = American Gastroenterological Association; anti-HBc = hepatitis B core antibody; anti-HBs = hepatitis B surface antibody; ASCO = American Society of Clinical Oncology; CDC = Centers for Disease Control and Prevention; DGHO = German Society for Haematology and Medical Oncology; EASL = European Association for the Study of the Liver; ECCO = European Crohn´s and Colitis Organisation; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HBV DNA = hepatitis B virus DNA; HBVr = hepatitis B reactivation; IBD = inflammatory bowel disease

Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update

Chronic HBV infection: HBsAg seropositive status at 6 months or beyond

Low replicative chronic HBV infection: HBsAg(+) anti-HBe(+) with PNALT and HBV DNA <2000 IU/ ml and no liver injury (inactive carrier) or (inactive chronic HBV infection)

Chronic hepatitis B: chronic necroinflammatory disease of the liver caused by persistent infection with HBV. It can be subdivided into HBeAg-positive and HBeAg-negative chronic hepatitis B (CHB)

Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update

Resolved hepatitis B: previous HBV infection with a current state of HBsAg(-) and antiHBs(+)

Acute exacerbation or flare of hepatitis in chronic HBV-infected patient: intermittent elevations of serum aminotransferase level to more than 5 times the upper limit of normal and more than twice the baseline value

Reactivation of hepatitis: marked increase in HBV replication (=>2 log increase from baseline levels or a new appearance of HBV DNA to a level of =>100 IU/ml) in a person with previously stable or undetectable levels, or detection of HBV DNA with a level =>20,000 IU/ml in a person with no baseline HBV DNA

Table 2 Terminologies related to HBV infection

Terminology	Definition
ALT level	
High normal	Serum ALT between 0.5 and 1× upper limit of laboratory reference (ULN)
Low normal	Serum ALT ≤0.5× ULN
Minimally raised	Serum ALT between ULN and 2× ULN
Raised	Serum ALT 2× ULN
Chronic HBV infection	HBsAg seropositive status beyond 6 months
Low replicative chronic HBV infection	HBsAg(+), HBeAg(−) anti-HBe(+) status with persistent normal serum ALT, HBV DNA <2000 IU/ml and no evidence of liver injury
Incidentally detected HBsAg positive subject (IDAHS)	An asymptomatic individual who has been found to be HBsAg positive on routine blood screening. Such a subject could have different levels of HBV DNA and could have no evidence of liver disease to varied stages of liver disease, and hence needs to be worked up
Chronic hepatitis B	Chronic necroinflammatory disease of liver caused by persistent infection with hepatitis B virus. It can be subdivided into HBeAg-positive and HBeAg-negative chronic hepatitis B
Resolved hepatitis B infection	Previous HBV infection, but now HBsAg(−) and anti-HBs(+)
Acute exacerbation or flare of hepatitis B	Intermittent elevations of aminotransferase to more than 5 times the upper limit of normal and more than twice the baseline value
Reactivation of hepatitis B	Reappearance of active necroinflammatory disease of liver in a patient known to have the inactive chronic HBV infection state or resolved hepatitis B infection
HBeAg clearance	Loss of HBeAg in a person who was previously HBeAg positive
HBeAg seroconversion	Loss of HBeAg and detection of anti-HBe in a person who was previously HBeAg positive and anti-HBe negative
HBeAg reversion	Reappearance of HBeAg in a person who was previously HBeAg negative, anti-HBe positive
Hepatic decompensation	Defined as significant liver dysfunction as indicated by raised serum bilirubin (more than 2.5 times the upper limit of normal) and prolonged prothrombin time (prolonged by more than 3 s), or INR >1.5 or occurrence of complications such as ascites and hepatic encepahalopathy
Undetectable serum HBV DNA	Serum HBV DNA below detection limit of a PCR-based assay

Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update

HBsAg+ individuals who are candidates for immunosuppressive therapy should receive antiviral prophylaxis at the onset of treatment, and maintain this for 6-12 months after the conclusion of treatment.

The guidelines also recommend testing for HBV markers (HBsAg, anti-HBs, and anti-HBc).

Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update

HBs Ag-negative patients with positive anti-HBc antibodies should be tested for HBV DNA:

- If had **detectable** serum HBV DNA should be treated similarly to HBsAg positive patients.

- If had **undetectable** serum HBV DNA, and who receive immunosuppression regardless of anti-HBs status, should be followed carefully by means of ALT and HBV DNA testing, and be treated with NA therapy upon confirmation of HBV reactivation before ALT elevation

Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update

The frequency of monitoring can range from 1 to 3 months, depending on the type of immunosuppressive therapy and comorbidities.

Some experts recommend prophylaxis in all ***HBsAg-negative, anti-HBc positive*** patients who receive rituximab if they are anti-HBs negative and/or if close monitoring of HBV DNA is not guaranteed

Biologics with hepatitis B or C: recommendation

Screening for HBS Ag:

- If there is evidence of past or present HBV infection, the quantitative HBV-DNA viral load should be determined and prophylactic antiviral therapy should be given

- Patients with resolved HBV infection (i.e., HBc-antibody-positive, normal liver function tests, HBc-antibody-positive, and HBsAg-negative) should receive the same biological treatment as unexposed patients as long as the patient's viral load is monitored regularly (i.e., at least every 6–12 months).

Biologics with hepatitis B or C: recommendation

Of all cases published in the literature up to 2012 identified 25 HBsAg-positive patients suffering from rheumatic disease treated by anti-TNF without antiviral prophylaxis

HBV reactivation occurred in 13 cases, including three cases that resulted in fulminant hepatitis, one death, and one liver transplantation, which may alternatively have been related to Still's disease or an idiopathic drug reaction.

Biologics with hepatitis B or C: recommendation

Infliximab is associated with a greater risk of reactivation of HBV in HBsAg-positive patients compared with etanercept or adalimumab

The risk of HBV reactivation in HBsAg-negative/anti-HBc-positive patients is low

In a literature review, Vigano showed a total of 214 patients suffering from rheumatological disorders or IBD with HBsAg-negative/HBc-antibody-positive carriers were treated with IFX, ETN, and ADA. In only three cases with reported HBV reactivation followed by a hepatitis flare-up, the drug was withdrawn and antiviral medication started.

Biologics with hepatitis B or C: recommendation

The currently recommended protocol includes prophylaxis with lamivudine of all inactive carriers (HBsAg negative HBc antibody positive patients) during therapy and for 6–12 months following therapy with TNF-α inhibitors and quarterly monitoring of HBsAg

The 2008 guidelines of the ACR, updated in 2012, do not recommend the use of anti-TNF-α in pharmacologically untreated chronic hepatitis B and treated with considerable damage to the liver.

If during treatment with anti-TNF-α patient is diagnosed with hepatitis B, you can implement an antiviral drug

Biologics with hepatitis B or C: recommendation

During therapy, patients should be monitored for HBV DNA (every 3–6 months) and ALT (every 3 months)

Tenofovir or entecavir is a good choice among active carriers with high HBV DNA in the case of reactivation or development of hepatitis

Lamivudine is recommended as prophylaxis in inactive and hidden carriers

Biologics with hepatitis B or C: recommendation

The risk of *HCV* infection flareup during anti-TNF treatment is controversial.

In a comprehensive literature review conducted by Pompili et al. between January 2000 and August 2013, a total of 216 patients with HCV were observed for a cumulative total of 260 patients / years of anti-TNF treatment. Only three cases of drug withdrawal due to suspected worsening of HCV liver were reported.

Short-term use of anti-TNF appears safe, but insufficient long-term safety data exist.

Rheumatologists should collaborate with the hepatologists to determine if the patient is a candidate for antiviral treatment

Biologics with hepatitis B or C: recommendation

Biologics such as anti-TNF and RTX have been usefully employed without significant side effects in ***HCV-RNA-positive*** RA patients.

Due to the lack of sufficient prospective studies demonstrating the rate of HCV flare-up on biological therapy, caution should be exercised and careful monitoring of liver enzymes and viral load is mandated in vulnerable HCV-RNA patients.

The novelty in relation to the recommendations of the ACR 2008 is to allow the possibility of the use of etanercept in the treatment of RA patients with hepatitis C

Cirrhosis

In compensated cirrhosis: anti-TNF drugs should be used with caution and the benefit:risk ratio evaluated at the individual level

decompensated liver disease : anti-TNF drugs contraindicated

Glucocorticoids

For the treatment of longer than 2 weeks, the dose above 20 mg/day of prednisolone or its equivalent is generally considered clinically significant to induce immunosuppression

But has been shown that the cumulative dose of 500 mg or below the average daily dose of less than 10 mg of prednisolone does not increase the risk of infectious complications, and can be stated that are potent immunosuppressive

Non-biological DMARD

Is relatively safe in patients with a low risk of reactivation—a low level of HBV DNA, anti-HBs (+) and the use of prophylaxis in these patients are not recommended.

There are also isolated reports of HBV reactivation during treatment MTX , leflunomide, azathioprine, chloroquine and sulfasalazine .

At the same time, there are early reports on the role of sulfasalazine in the intensification of apoptosis of cells secreting antigen HBV

Currently, there are no formal guidelines on eligibility for treatment of HBV patients with Rituximab, Abatacept and Tocilizumab.

In these patients, it is recommended the initial determination of the presence of HBsAg and anti-HBc and anti-HBs.

Patients with current HBs antigen should receive antiviral treatment.

Available data on this subject for rituximab in rheumatic diseases are limited, and for tocilizumab and abatacept inaccessible

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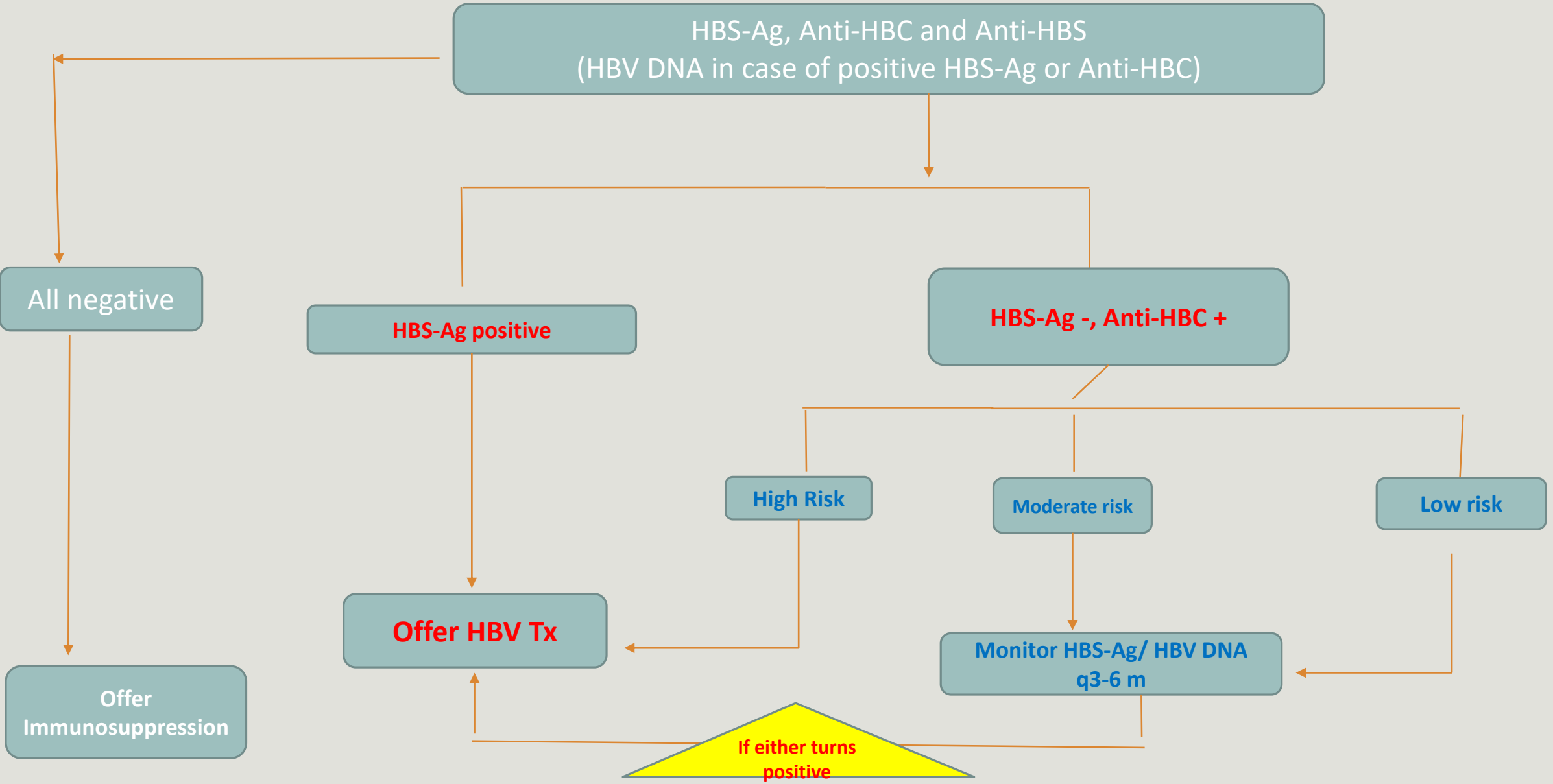
Risk of hepatitis B virus reactivation stratified by immunosuppressive regimen

	HBsAg positive	HBsAg negative – anti-HBc positive
High risk >10%	• B-cell depleting agents (eg rituximab, ofatumumab) • Anthracycline derivatives (eg doxorubicin, epirubicin) • Moderate (prednisolone 10–20 mg daily or equivalent) or high-dose (prednisolone >20 mg daily or equivalent) corticosteroids daily for ≥4 weeks • Potent TNF-α inhibitors, including adalimumab, certolizumab, infliximab and golimumab • Local treatment for HCC, including TACE	• B-cell depleting agents (eg rituximab, ofatumumab)
Moderate risk 1-10%	• Less potent TNF-α inhibitors (eg etanercept) • Cytokine or integrin inhibitors (eg abatacept, ustekinumab, natalizumab, vedolizumab) • Tyrosine kinase inhibitors (eg imatinib,	• TNF-α inhibitors (eg etanercept, adalimumab, certolizumab, infliximab) • Cytokinee or integrin inhibitors (eg abatacept, ustekinumab, natalizumab, vedolizumab) • Tyrosine kinase inhibitors (eg imatinib,


HBS-Ag, Anti-HBC and Anti-HBS
(HBV DNA in case of positive HBS-Ag or Anti-HBC)
All negative
HBS-Ag positive
HBS-Ag -, Anti-HBC +
High Risk
Moderate risk
Low risk
Offer HBV Tx
Monitor HBS-Ag/ HBV DNA q3-6 m
Offer Immunosuppression
If either turns positive

RA and cancer

- A meta-analysis reported that patients with RA have a 10% increase in the overall malignancy risk compared with the general population
- Because both RA and cancer require aggressive and often long-term treatment, ensuring that the management of each condition does not interfere with the outcomes of the other is key

Incidence of malignancy in adult patients with rheumatoid arthritis: a meta-analysis, Teresa A. Simon, Adam Thompson, Kunal K. Gandhi,Marc C. Hochberg & Samy Suissa *Arthritis Research & Therapy* **volume 17**, Article number: 212 (2015)

RA and cancer

The mechanism by which immunosuppressants promote cancer includes direct alterations of DNA in cells, reduced immunosurveillance for tumor cells, or impaired immunosurveillance for chronic infection by mutagenic viruses

RA and cancer

- **Studies**
- **Systematic reviews**
- **ACR**
- **EULAR**
- **APLAR**
- **Canadian Dermatology-Rheumatology Comorbidity Initiative**

Anti-TNF antibody therapy in RA and the risk of serious infections and malignancies: systematic review and meta-analysis of rare harmful effects in randomized controlled trials Tim Bongartz rt al; JAMA. 2006 Jun 7;295(21):2482

- Previous studies have evaluated the risk of incident cancer development among individuals exposed to anti-TNF therapy. In an early meta-analysis of data from randomized controlled trials utilizing anti-TNF therapy in individuals with RA, Bongartz et al., demonstrated a dose-dependent increased risk of malignancy among individuals exposed to anti-TNF therapy (pooled OR 3.3, 95% CI 1.2–9.1)
- However, the initial meta-analysis suggesting an increased risk of incident cancer development was critiqued citing an unexpectedly low rate of malignancy in the control arms of the meta-analysis, the use of an odds ratio to compare malignancy risk as opposed to incidence rates, therefore assuming equality of patient follow-up, as well as inclusion of malignancy diagnosed within six weeks of therapy initiation

Influence of Anti–Tumor Necrosis Factor Therapy on Cancer Incidence in Patients With Rheumatoid Arthritis Who Have Had a Prior Malignancy: Results From the British Society for Rheumatology Biologics Register W. G. DIXON, Arthritis Care & Research Vol. 62, No. 6, June 2010, pp 755–763

- We have shown that in patients with RA and prior malignancy, the rate of incident malignancy is not increased in patients selected to receive anti-TNF therapy after an average of 3 years of followup
- In summary, we have shown that the way in which UK rheumatologists are selecting their patients with RA and prior malignancy to receive anti-TNF therapy is not leading to an increased risk of incident malignancy over the period of followup studied. The results should not be interpreted as indicating that it is safe to treat all RA patients with prior malignancy with anti-TNF therapy.

Risk of Cancer Recurrence Among Individuals Exposed to Anti-TNF Therapy: A Systematic Review and MetaAnalysis of Observational Studies

Dejan Micic, MD et al; J Clin Gastroenterol. 2019 January ; 53(1): e1–e11

- Data Sources: We performed a computerized literature search of EMBASE (1947–September 2015), MEDLINE (1981–September 2015), Google scholar (1981–September 2015), and Cochrane Database of Systematic Reviews (2009–September 2015).
- We also searched abstracts from scientific meetings: American Gastroenterology Association (2010–2015), American College of Gastroenterology (2006–2015), United European Gastroenterology, 2013–2014), American College of Rheumatology (2010–2014), European League Against Rheumatism (2002–2015), American Academy of Dermatology (2009–2015) and bibliographies of identified articles for additional references.

Risk of Cancer Recurrence Among Individuals Exposed to Anti-TNF Therapy: A Systematic Review and MetaAnalysis of Observational Studies

Dejan Micic, MD et al; J Clin Gastroenterol. 2019 January ; 53(1): e1–e11

- The search strategy identified 4,425 citations, of which 4,292 records were excluded after examining the title and abstract. Ninety-two studies were retrieved and evaluated in detail.
- We found that the risk of new or recurrent cancer among individuals with a history of cancer exposed to anti-TNF therapy was not significantly different compared to control therapies.
- We have demonstrated that patients with a history of cancer are not at an increased risk of developing a new or recurrent cancer when exposed to anti-TNF therapy when compared to a comparator population receiving non-biologic disease modifying therapies.
-

Risk of Cancer Recurrence Among Individuals Exposed to Anti-TNF Therapy: A Systematic Review and MetaAnalysis of Observational Studies

Dejan Micic, MD et al; J Clin Gastroenterol. 2019 January ; 53(1): e1–e11

- In terms of individual cancer types studied, there were no obvious differences in risk of new cancer development or cancer recurrence among individuals with a history of solid tumor malignancy, skin cancer, or when examining the subgroup excluding skin cancers.
- this meta-analysis including 10 study populations and over 3,500 patients with a history of anti-TNF use after cancer diagnosis demonstrates the safety of anti-TNF therapy among individuals with a history of cancer, without a demonstrated risk for the development of new or recurrent cancer compared to non-biologic disease modifying therapies.
- Given the prolonged interval between cancer diagnosis and anti-TNF initiation in most studies, care should still be taken with a multi-disciplinary approach to adequately discuss with the patient and treating physician risk of individual disease recurrence and the known risks and benefits of anti-TNF therapy for modifying clinical disease activity

Rheumatoid arthritis treatment in patients with a history of cancer
Anne C. Regierer and Anja Strangfeld, COR 2018

- The question of the best RA treatment option for patients with a history of cancer is not yet answered satisfactorily.
- Randomized clinical trials are an inadequate study type in this regard: their follow-up is too short and most of them exclude patients with a history of cancer. Therefore, available evidence is scarce and relies solely on observational data.

Does cancer that occurs during or after anti-TNF therapy have a worse prognosis? A national assessment of overall and site-specific cancer survival in RA patients treated with biologic agents

- When cancer develops among individuals exposed to anti-TNF therapies,no increased risk of death was demonstrated among individuals developing cancer while on anti-TNF therapy compared to a biologics-naïve control group
- For all cancers combined, the distribution of cancer stages at the time of cancer diagnosis was largely similar between those in the biologics-exposed and the matched groups.
- During routine care, cancers that occur following anti-TNF therapy are not characterized by any markedly altered stage at presentation or by altered post-cancer survival rates.

Systematic Review of Recommendations on the Use of DMARDs in Patients With RA and Cancer , Maria A. Lopez-Olivo,1 Inés Colmegna, Arthritis Care & Research Vol. 72, No. 3, March 2020, pp 309–318

Objective: To evaluate consensus recommendations regarding management of RA in patients with cancer.

Methods: We searched electronic databases, guideline registries, and relevant web sites for cancer-specific recommendations on RA management.

Results: Of 4,077 unique citations, 39 recommendations were identified, of which half described their consensus process

Conclusion: Recommendations for the treatment of RA in patients with cancer often fail to meet expected methodologic criteria. There was agreement on the need for caution when prescribing DMARDs to these patients. However, several areas continue to lack consensus, and given the paucity of evidence, there is an urgent need for research and expert opinion to guide and standardize the management of RA in patients with cancer

Systematic Review of Recommendations on the Use of DMARDs in Patients With RA and Cancer , Maria A. Lopez-Olivo,1 Inés Colmegna, Arthritis Care & Research Vol. 72, No. 3, March 2020, pp 309–318

- Currently, 39 consensus recommendations cover at least 1 area related to cancer risk screening and/or monitoring or the management of patients with a current or past history of cancer.
- Most recommendations caution about an increased probability of cancer risk in patients with RA and a possible association between some DMARDs and specific cancers.
- Regarding screening, most recommendations were in favor of screening for age-prevalent cancer types prior to RA treatment initiation.
- For monitoring, the broad consensus was for ongoing monitoring of possible cancer symptoms during RA treatment. However, recommendations did not provide guidance on specific screening tests.

Systematic Review of Recommendations on the Use of DMARDs in Patients With RA and Cancer , Maria A. Lopez-Olivo,1 Inés Colmegna, Arthritis Care & Research Vol. 72, No. 3, March 2020, pp 309–318

- For the management of patients with cancer, most agreed that DMARD treatment should be stopped and only resumed in consultation with a specialist in the case of de novo cancer.
- It was not recommended to initiate RA treatment in patients with active cancer or premalignant conditions
- Regarding a prior history of cancer, most recommendations advised caution when prescribing DMARDs, particularly when the cancer was treated within the past 5 years.
- Most cautioned against the prescription of TNFi for these patients, especially when the cancer in question was lymphoma or other hematologic malignancy.
- Many recommendations considered rituximab as an adequate bDMARD choice

Systematic Review of Recommendations on the Use of DMARDs in Patients With RA and Cancer , Maria A. Lopez-Olivo,1 Inés Colmegna, Arthritis Care & Research Vol. 72, No. 3, March 2020, pp 309–318

- We did not find consensus in terms of treatment of RA in patients at risk of cancer. In general, earlier recommendations were more conservative, contraindicating DMARDs, particularly bDMARDs, whereas more recent recommendations advised caution in prescribing, but not absolute contraindication.
- Cancer specific advice (site, stage) in the included recommendations were vague, possibly reflecting the lack of evidence
-

APLAR rheumatoid arthritis treatment recommendations

- No consensus about Malignancy
- Rituximab may be used in RA patients with lymphoma
- Special comment/recommendation for the AP region It is of particular importance that clinicians have a high level of alertness of pre-existing infectious diseases, including uncommon infections, and other comorbidities in AP patients receiving bDMARDs because of differences in the pattern and frequency of occurrence of these conditions in this region

BSR

- Patients commencing anti-TNF should be informed that overall there is no conclusive evidence for an increase in risk of solid tumours or lymphoproliferative disease above that expected for the rest of the RA population, but ongoing vigilance is required.
- Patients should be investigated for potential malignancy if clinically suspected, and anti-TNF should be stopped if malignancy is confirmed.
- Caution should be exercised in the use of anti-TNF in patients with previous malignancy.
- The effect of anti-TNF on pre-malignant conditions is unknown. Caution should be exercised in the use of anti-TNF in such patients.
- Patients should be advised that there appears to be an increased risk of some skin cancers with anti-TNF and on preventative skin care and skin surveillance. Patients should promptly report any new persistent skin lesions.

Expert Opinion of the Canadian Dermatology-Rheumatology Comorbidity Initiative

- Prior to initiating systemic therapy, additional cancer screening beyond the nationally recommended guidelines for age and sex is not required. Individuals at increased risk for skin cancer may require closer monitoring (Grade of Recommendation: C).
- Our meta analysis in subjects treated with systemic therapy found an overall RR of malignancy of 1.25 (95% CI 0.88–1.78) in RA and 1.12 (95% CI 0.88–1.42) in PsO. The RR of malignancy could not be estimated in PsA because of the lack of data. The initiation of TNFi was not associated with an increased incidence of overall malignancy in RA (RR 1.29, 95% CI 0.88–1.89) and could not be estimated in PsA or PsO because of insufficient data

Expert Opinion of the Canadian Dermatology-Rheumatology Comorbidity Initiative

- Although site-specific malignancy analysis was not performed, previous studies have shown that the risk of non-melanoma skin cancer and melanoma may be increased, particularly in RA. TNFi may contribute to this increased risk, but results are not consistent
- In the absence of sufficient data on recurrent cancer, patients with a prior cancer should be informed about a potential risk of new or recurrent cancer when treated for RA, PsA, or PsO with TNFi or some of the DMARD (Grade of Recommendation: C)
- Although current studies did not demonstrate an increased RR of recurrent or new cancer, the expert panel felt that patients treated with TNFi should be aware that they may have an increased risk of recurrent malignancy, this risk being difficult to quantify because of insufficient data from studies that included a very limited number of patients with prior cancer.

ACR 2015

Past history of treated or untreated malignancy[4]		
Previously treated or untreated skin cancer (non-melanoma or melanoma)	*Use DMARDs over biologics in melanoma (PICO F.1).* *Use DMARDs over tofacitinib in melanoma (PICO F.2).* *Use DMARDs over biologics in non-melanoma (PICO F.3).* *Use DMARDs over tofacitinib in non-melanoma (PICO F.4).*	*Very low (104-106)*
Previously treated lymphoproliferative disorder	**Use rituximab over TNFi (PICO G.1).**	**Very low (105,107)**
Previously treated lymphoproliferative disorder	*Use combination DMARD or abatacept or tocilizumab over TNFi* (PICO G.2, G.3 and G.4).	*Very low (105,107)*
Previously treated solid organ malignancy	*Same recommendations as in patients without this condition (PICO H.1).*	*Very low (105,108)*

ACR 2015

PICOS F.1, F.2, F.3, AND F.4.

- The recommendation is conditional because

  1) the evidence is of very low quality

  2) due to potentially lower risk of recurrence of skin cancer with DMARDs versus other therapies based on clinical experience and 2 retrospective studies

  3) a lack of data and knowledge about some of the mechanisms of action of biologics and tofacitinib, which may potentially contribute to an increased cancer risk.

- DMARDs were considered less immunosuppressive than biologics.
- Host factors may vary and may influence the risk of recurrence of skin cancer.
- Even though biologics were not the first option, several Voting Panel members indicated that if the joint disease was moderately or highly active in the setting of a low grade melanoma or non-melanoma skin cancer that had been previously treated, biologics would be an acceptable option with close skin surveillance in conjunction with a dermatologist.

Past history of treated or untreated malignancy[4]		
Previously treated or untreated skin cancer (non-melanoma or melanoma)	*Use DMARDs over biologics in melanoma (PICO F.1).* *Use DMARDs over tofacitinib in melanoma (PICO F.2).* *Use DMARDs over biologics in non-melanoma (PICO F.3).* *Use DMARDs over tofacitinib in non-melanoma (PICO F.4).*	*Very low (104-106)*
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PICO G.1.

- The recommendation is strong despite very low quality evidence because rituximab is an approved treatment for some of these disorders and the best available clinical trial data suggest that there is a signal in clinical trials of induction and/ or an increased risk of lymphoma in patients treated with TNFi

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PICOS G.2, G.3, AND G.4.

- The recommendation is conditional because:

1) The evidence is of very low quality

2) There is a lack of evidence for combination DMARD therapy versus TNFi

3) There is a possible increased risk of lymphoma associated with TNFi, but there is no evidence that abatacept or tocilizumab increases this risk

- PICO H.1. The recommendation is conditional because the evidence is of very low quality

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ACR 2020 Recommnedation

- Final publication of updated guideline anticipated in fall 2020
- Project Plan – October 2018

EULAR: Updated consensus statement on tumour necrosis factor blocking agents for the treatment of rheumatoid arthritis (May 2000); Ann Rheum Dis 2000;59(suppl I):i1–i2

The effect of TNF blockade is unknown in the following situations: x Lymphoma, lymphoproliferative and other malignancies