BİYOLOJİK AJAN KULLANIMI VE ENFEKSİYONLARA YAKLAŞIM

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Başkent Üniversitesi Adana Dr. Turgut Noyan Uygulama ve Araştırma Merkezi

Enfeksiyon Hastalıklar ve Klinik Mikrobiyoloji AD

EKMUD Çukurova Günleri-18 ARALIK 2019


Biyolojik ajan
Konvansiyonel - Hastalık Modifiye Edici Anti-Romatizmal İlaçlar
Hedefe Yönelik- Hastalık Modifiye Edici Anti-Romatizmal İlaçlar
Hastalık Modifiye Edici Anti-Romatizmal İlaçlar
Hedefe yönelik tedavi
İmmunsupresif
Biyolojik - Hastalık Modifiye Edici Anti-Romatizmal İlaçlar

Hastalık Modifiye Edici Antiromatizmal İlaçlar (DMARD)

- Sentetik DMARD'lar (sDMARD'lar)
  - Konvansiyonel Sentetik (cs DMARD)
  - Hedefe Yönelik Sentetik (tsDMARD)
- Biyolojik DMARD'lar (bDMARD'lar)
  - Orijinal Biyolojik (bo DMARD)
  - Biyobenzer (bs DMARD)

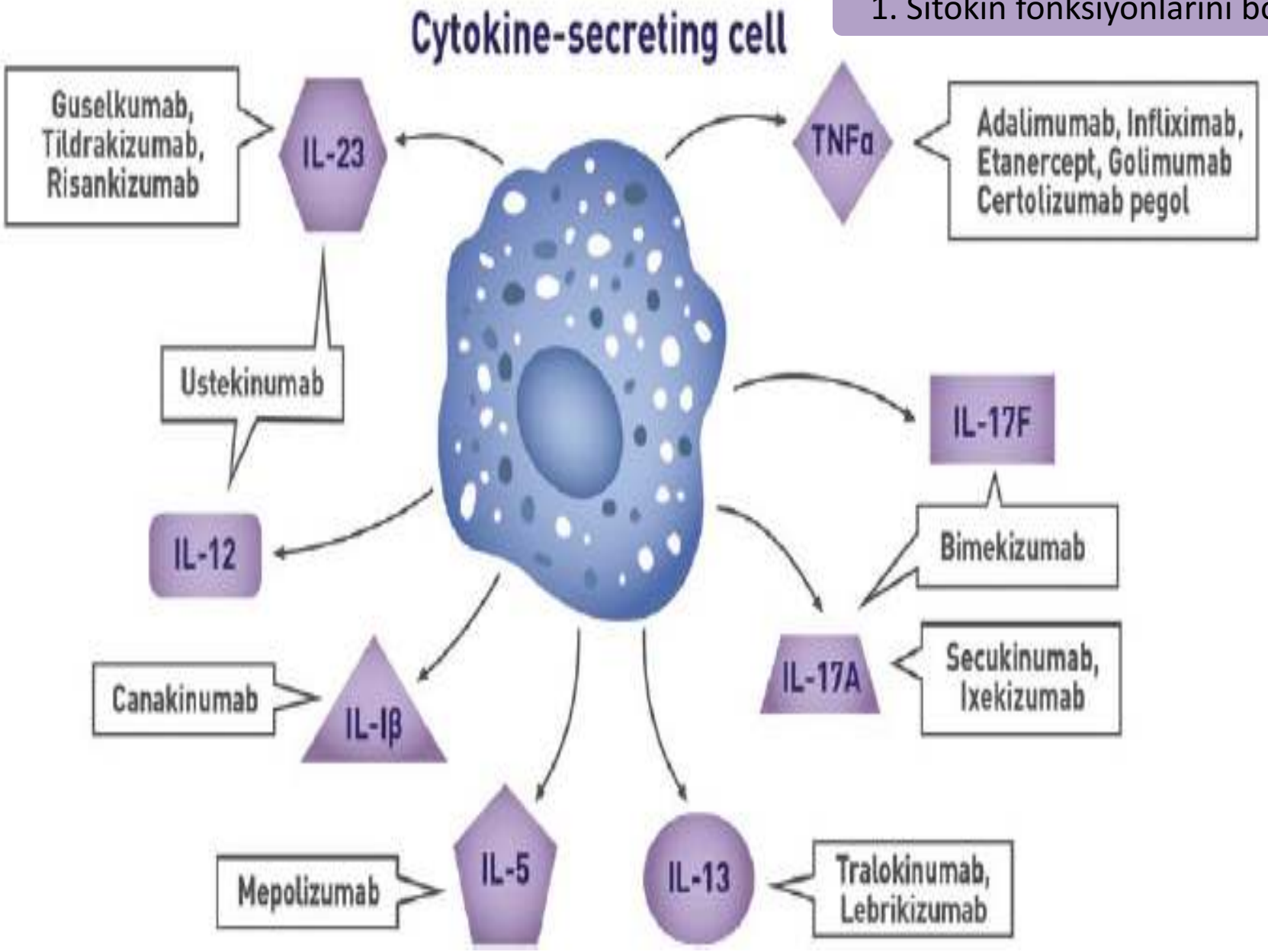
Smolen JS, et al. Ann Rheum Dis 2014;73:3-5.

RHEUMATOLOGY
Guidelines
British Society for Rheumatology
Rheumatology 2019;58:220–226
doi:10.1093/rheumatology/key207
Advance Access publication 21 August 2018

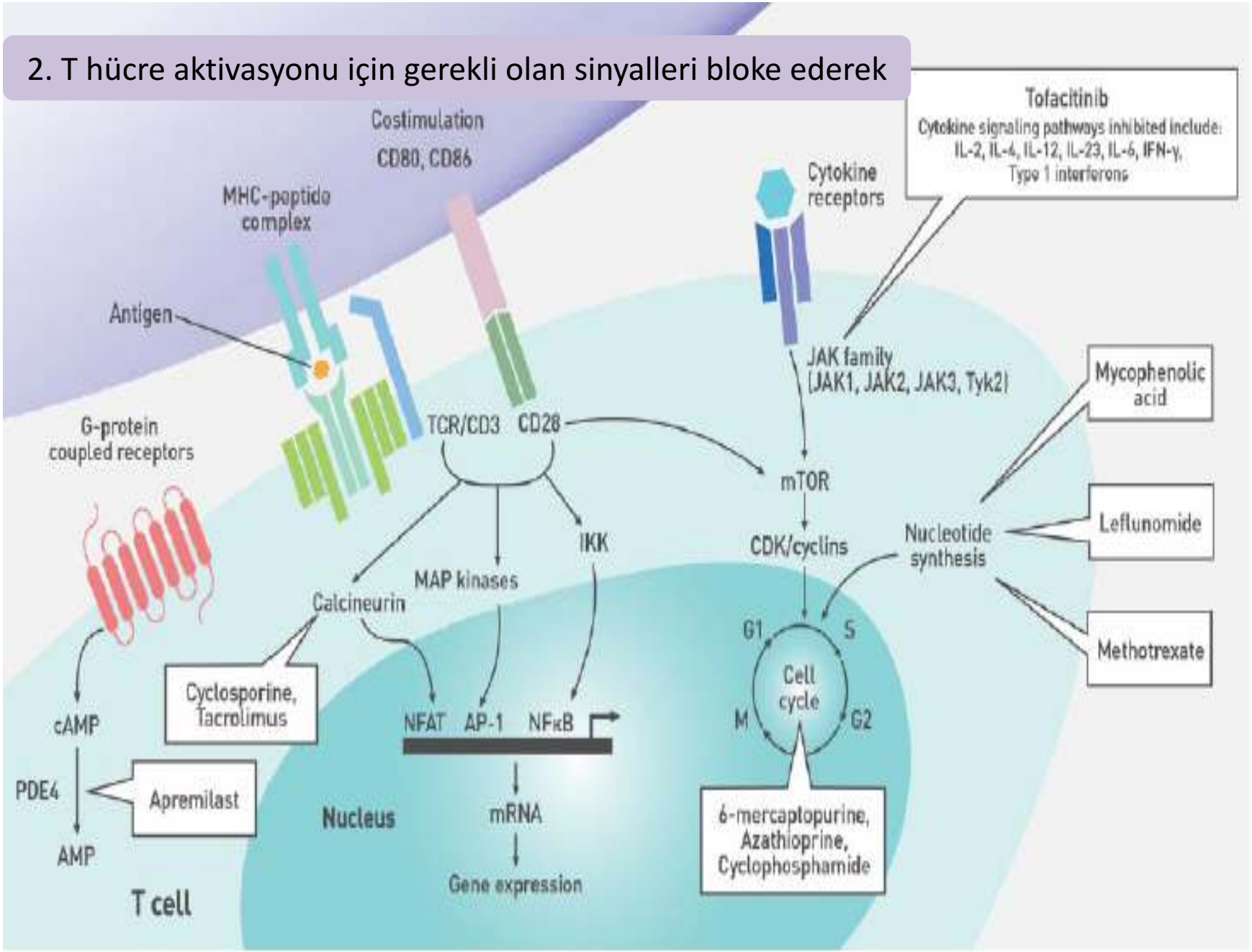
The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis—Executive summary

csDMARDs	boDMARDs	tsDMARDs
Methotrexate (MTX)	TNF Inhibitors	JAK Inhibitors
Hydroxychloroquine (HCQ)	• Etanercept	• Tofacitinib
Sulfasalazine (SSZ)	• Adalimumab	• Baricitinib
Leflunomide (LEF)	• Certolizumab	
	• Golimumab	
	• Infliximab	
	Abatacept	
	Rituximab	
	IL-6 Receptor Inhibitors	
	• Tocilizumab	
	• Sarilumab	

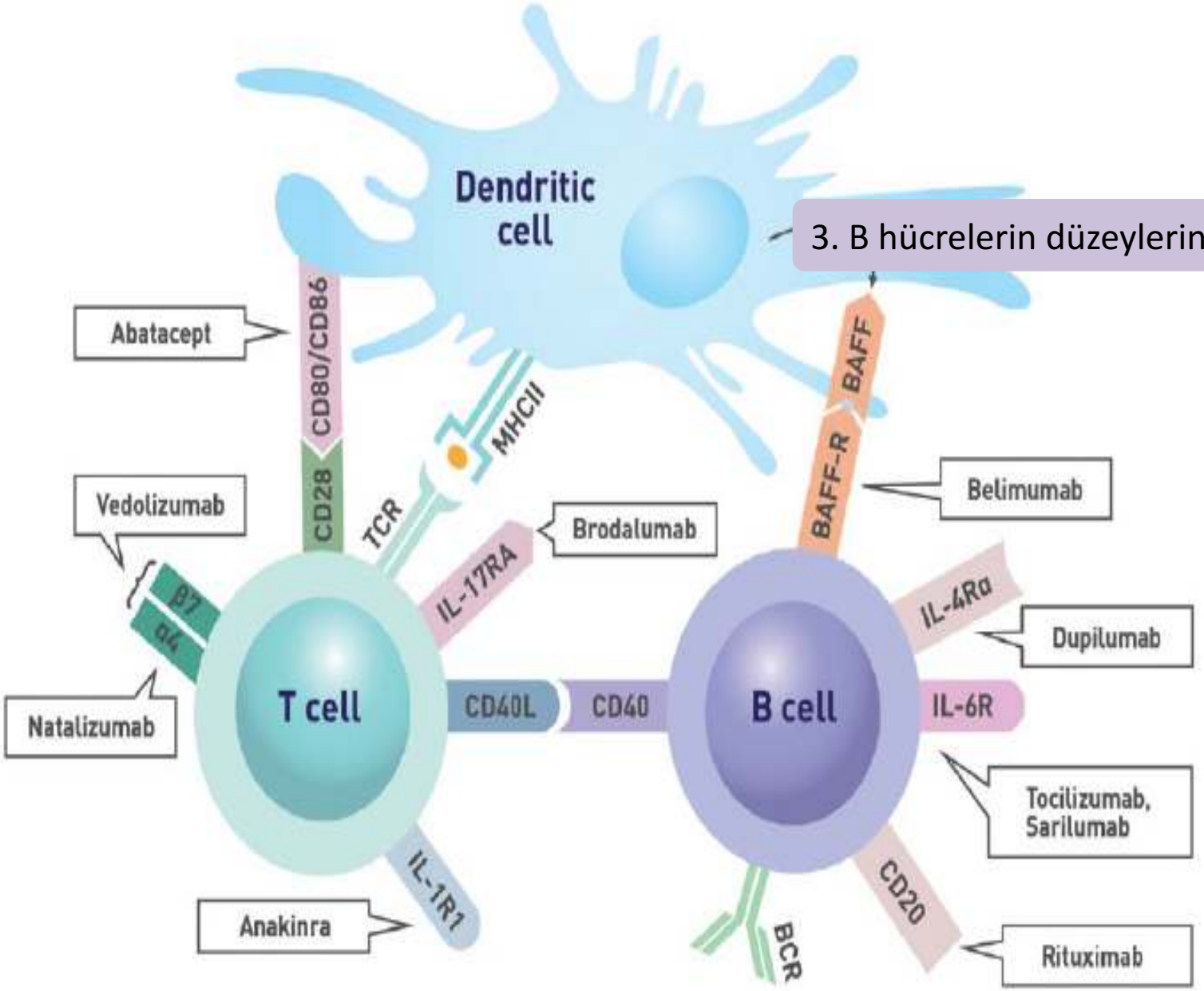
1. Sitokin fonksiyonlarını bozarak



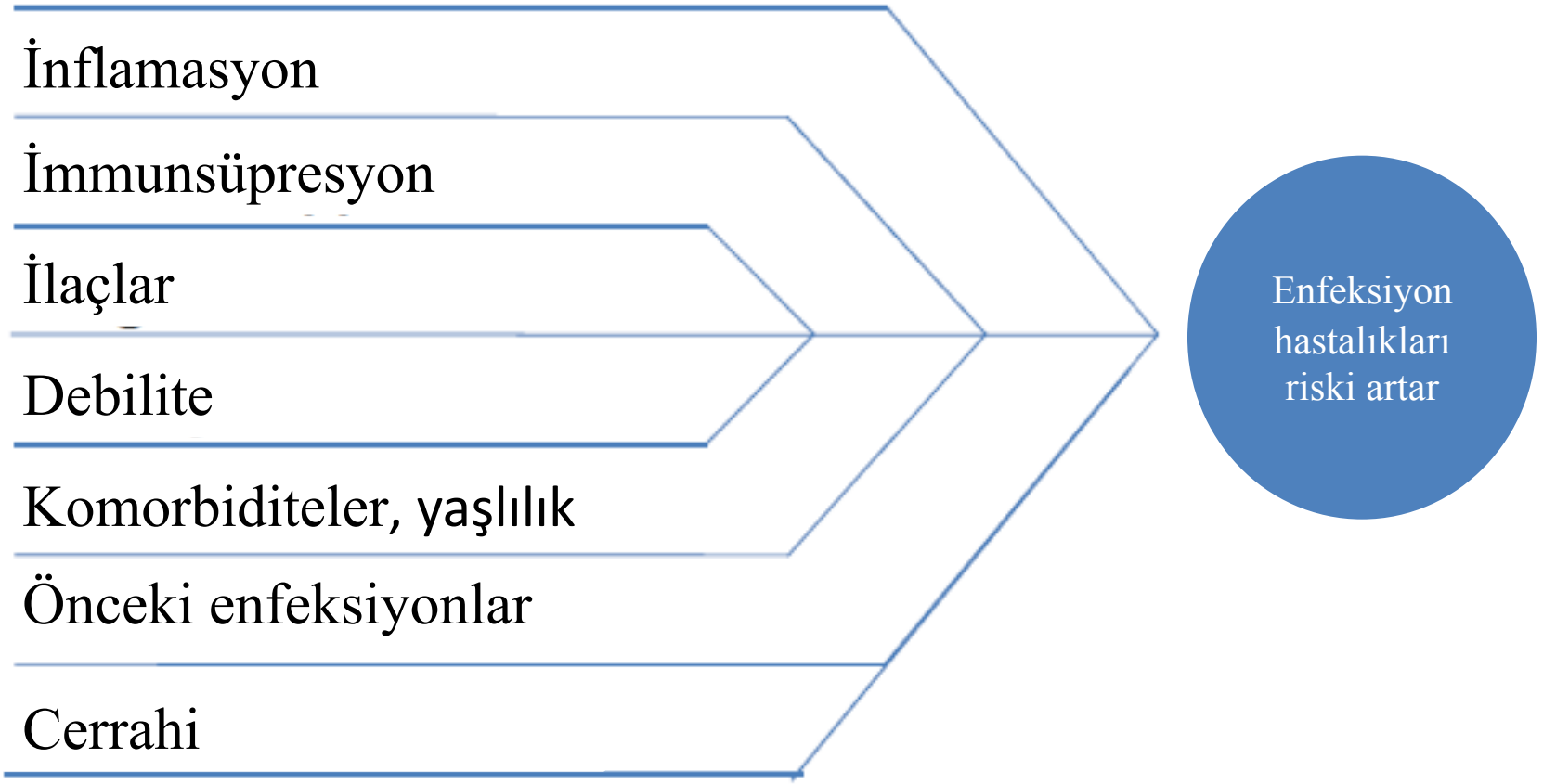
2. T hücre aktivasyonu için gerekli olan sinyalleri bloke ederek



3. B hücrelerin düzeylerini azaltarak



Biyolojik Ajan Kullanan Hastalarda Enfeksiyon Riski Yüksek mi?



Kaandorp CJ, Arthritis Rheum 1995;38:1819-25.
Doran Fl. Arthritis Rheum 2002;46:2287-93.

Arthritis Care & Research
DOI 10.1002/acr.22783
© 2015, American College of Rheumatology

SPECIAL A

2015 A Guide Arthri

JASVINDER
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CHRISTINE
DANIEL E. F
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AMY S. MIL

Guidelines (ACR) are i ticular patie with the ult patient's ina desirable ou and endorse technology, These recon

The ACR is endorse any

AMERICAN COLLEGE OF RHEUMATOLOGY

EDUCATION • TREATMENT • RESEARCH

American College Of Rheumatology

Updated Guideline for the Management of Rheumatoid Arthritis

Genel İlkeler

- Ciddi enfeksiyonlar ilk 3-6 ayda görülür.
- Ciddi infeksiyon (CE) durumunda biyolojik ilaçlar başlanmamalıdır.
- CE durumunda yarar ve zarar oranı göz önünde tutulup ilaç başlanabilir.
- CE durumunda ilk seçenek ilaç olarak ETN ya da ABA düşünülebilinir.
- Biyolojik ajan kullanımı esnasında CE gelişirse ilaç kesilmelidir.

Rheumatology 2019;58:220226

Biyolojik Ajanların Enfeksiyon Sıklığı ve Tipleri

Table 2 Incidence of serious infection by drug

	Etanercept	Infliximab	Adalimumab	Rituximab	Tocilizumab	Certolizumab
Number of patients	8630	4908	7818	5101	2174	1446
Follow-up time in years	15314	8829	13071	5910	1963	1685
Infections: single failure	852	472	709	372	137	64
Incidence per 100 patient years (95% CI)*	5.56 (5.20 to 5.95)	5.35 (4.89 to 5.85)	5.42 (5.04 to 5.84)	6.29 (5.69 to 6.97)	6.98 (5.90 to 8.25)	3.80 (2.97 to 4.85)
Unadjusted HR (95% CI)	Ref	0.94 (0.84 to 1.06)	0.97 (0.88 to 1.07)	1.15 (1.01 to 1.30)	1.22 (1.02 to 1.47)	0.65 (0.51 to 0.84)
Adjusted HR (95% CI)	Ref	0.89 (0.79 to 1.00)	1.00 (0.90 to 1.10)	0.91 (0.80 to 1.03)	1.21 (1.01 to 1.46)	0.75 (0.58 to 0.97)

Covariates included in the adjusted model were age, gender, Disease Activity Score 28-erythrocyte sedimentation rate, Health Assessment Questionnaire, disease duration, smoking, seropositivity, polypharmacy and baseline steroid usage.

*Unadjusted incidence

Rutherford AI, et al. Ann Rheum Dis 2018;77:905–910.

Biyolojik Ajanların Enfeksiyon Sıklığı ve Tipleri

Table 3 Adjusted relative risk of infection by organ class for each drug

Organ class	Etanercept	Infliximab	Adalimumab	Rituximab	Tocilizumab	Certolizumab
Number of patients	8630	4908	7818	5101	2174	1446
Sepsis/bacteraemia (95% CI)	Ref	0.83 (0.41 to 1.66)	1.04 0.57 to 1.91)	2.08 (1.14 to 3.80)	1.83 (0.63 to 5.35)	1.03 (0.24 to 4.41)
Respiratory (95% CI)	Ref	1.16 (0.96 to 1.39)	1.23 (1.04 to 1.45)	1.03 (0.83 to 1.28)	**1.61 (1.15 to 2.25)**	0.96 (0.63 to 1.46)
Skin (95% CI)	Ref	0.84 (0.66 to 1.06)	0.65 (0.52 to 0.82)	0.54 (0.39 to 0.75)	0.71 (0.40 to 1.24)	**0.27 (0.11 to 0.67)**
Gastrointestinal (95% CI)	Ref	0.95 (0.66 to 1.38)	0.77 (0.54 to 1.11)	0.93 (0.61 to 1.42)	1.45 (0.72 to 2.90)	0.51 (0.16 to 1.63)
Bone/joint (95% CI)	Ref	0.56(0.38 to 0.83)	0.80 (0.58 to 1.09)	0.67 (0.43 to 1.02)	0.46 (0.17 to 1.27)	0.73 (0.32 to 1.68)
Genitourinary (95% CI)	Ref	0.74 (0.50 to 1.07)	1.18 (0.87 to 1.59)	1.15 (0.79 to 1.68)	0.67 (0.27 to 1.66)	0.55 (0.20 to 1.52)
Other (95% CI)	Ref	0.54 (0.31 to 0.91)	1.08 (0.74 to 1.58)	0.72 (0.41 to 1.29)	1.15 (0.49 to 2.67)	0.50 (0.16 to 1.60)

Rutherford AI, et al. Ann Rheum Dis 2018;77:905–910.

Fırsatçı Enfeksiyonlar

- Gözlemsel çalışmalar artmış fırsatçı enfeksiyon riskini ortaya koyuyorlar.
- Amerikan kohortunda herhangi bir risk artışı yok.
- Herhangi bir tarama, ampirik anti fungal tedavi önerilmiyor.
- Etanercept fırsatçı fungal enfeksiyon gelişimi açısından daha güvenlidir.
- FDA 2011 yılında tüm TNF alfa inhibitörleri için listeryoz ve lejyonelloz riski hakkında uyarı eklemiştir.

Ann Rheum Dis. 2011; 70:616-623.
Mayo Clin Proc. 2008; 83:181-194 .
Ann Rheum Dis. 2010; 69(2):380-386.

Clin Microbiol Infect. 2018 Jun;24 Suppl 2:S95-S107. doi: 10.1016/j.cmi.2018.01.030. Epub 2018 Feb 7.

ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an infectious diseases perspective (Immune checkpoint inhibitors, cell adhesion inhibitors, sphingosine-1-phosphate receptor modulators and proteasome inhibitors).

Redelman-Sidi G[1], Michielin O[2], Cervera C[3], Ribi C[4], Aguado JM[5], Fernández-Ruiz M[5], Manuel O[6].

Author information

Abstract

BACKGROUND: The present review is part of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Infections in Compromised Hosts (ESGICH) consensus document on the safety of targeted and biological therapies.

AIMS: To review, from an infectious diseases perspective, the safety profile of immune checkpoint inhibitors, LFA-3-targeted agents, cell adhesion inhibitors, sphingosine-1-phosphate receptor modulators and proteasome inhibitors, and to suggest preventive recommendations.

SOURCES: Computer-based Medline searches with MeSH terms pertaining to each agent or therapeutic family.

CONTENT: T-lymphocyte-associated antigen 4 (CTLA-4) and programmed death (PD)-1/PD-1 ligand 1 (PD-L1)-targeted agents do not appear to intrinsically increase the risk of infection but can induce immune-related adverse effects requiring additional immunosuppression. Although $CD4^+$ T-cell lymphopenia is associated with alefacept, no opportunistic infections have been observed. Progressive multifocal leukoencephalopathy (PML) may occur during therapy with natalizumab (anti-α4-integrin monoclonal antibody (mAb)) and efalizumab (anti-CD11a mAb), but no cases have been reported to date with vedolizumab (anti-α4β7 mAb). In patients at high risk for PML (positive anti-JC polyomavirus serology with serum antibody index >1.5 and duration of therapy ≥48 months), the benefit-risk ratio of continuing natalizumab should be carefully considered. Fingolimod induces profound peripheral blood lymphopenia and increases the risk of varicella zoster virus (VZV) infection. Prophylaxis with (val)acyclovir and VZV vaccination should be considered. Proteasome inhibitors also increase the risk of VZV infection, and antiviral prophylaxis with (val)acyclovir is recommended. Anti-Pneumocystis prophylaxis may be considered in myeloma multiple patients with additional risk factors (i.e. high-dose corticosteroids).

IMPLICATIONS: Clinicians should be aware of the risk of immune-related adverse effects and PML in patients receiving immune checkpoint and cell adhesion inhibitors respectively.

Enfeksiyon hastalıkları uzmanları, hematologlar, onkologlar, romatologlar ve daha birçok branş hekiminin dahil olduğu

- Her grup/ilaç için
- Etki mekanizması
- Onaylı kullanımı, endikasyon dışı kullanımı
- Konakta immünite üzerine beklenen etkileri
- Klinik veriler
- Öneriler

Clin Microbiol Infect. 2018 Jun;24 Suppl 2:S10-S20. doi: 10.1016/j.cmi.2017.12.025. Epub 2018 Feb 6.

ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an infectious diseases perspective (Soluble immune effector molecules [I]: anti-tumor necrosis factor-α agents).

Baddley JW[1], Cantini F[2], Goletti D[3], Gómez-Reino JJ[4], Mylonakis E[5], San-Juan R[6], Fernández-Ruiz M[6], Torre-Cisneros J[7].

Author information

TNF alfa inhibitöreri:

- ✓ İnfliximab
- ✓ Etanercept
- ✓ Adalimumab
- ✓ Golimumab
- ✓ Sertolizumab pegol

Abstract

BACKGROUND: The present review is pa ed Hosts (ESGICH) Consensus Document on the safety of targeted and b

AIMS: To review, from an Infectious Disea ur necrosis factor-α (TNF-α) and to suggest preventive recommendations.

SOURCES: Computer-based MEDLINE s apeutic family.

CONTENT: Preclinical and clinical evidenc , golimumab, certolizumab pegol and etanercept) is associated with a two-to fou granulomatous conditions (mostly resulting from the reactivation of a latent infection). In addition, it may lead to the occurrence of other serious infections (bacterial, fungal, opportunistic and certain viral infections). These associated risks seem to be lower for etanercept than other agents. Screening for latent tuberculosis infection should be performed before starting anti-TNF-α therapy, followed by anti-tuberculosis therapy if appropriate. Screening for chronic hepatitis B virus (HBV) infection is also recommended, and antiviral prophylaxis may be warranted for hepatitis B surface antigen-positive individuals. No benefit is expected from the use of antibacterial, anti-Pneumocystis or antifungal prophylaxis. Pneumococcal and age-appropriate antiviral vaccinations (i.e. influenza) should be administered. Live-virus vaccines (i.e. varicella-zoster virus or measles-mumps-rubella) may be contraindicated in people receiving anti-TNF-α therapy, although additional data are needed before definitive recommendations can be made.

IMPLICATIONS: Prevention measures should be implemented to reduce the risk of latent tuberculosis or HBV reactivation among individuals receiving anti-TNF-α therapy.

TNF alfa inhibitörleri

Adalimumab

Etanercept

Infliximab

Certolizumab

Golimumab

TNF alfa inhibitörleri

- ✓ IL-1 ve IL6 gibi proinflamatuvarsitokinlerin indüksiyonu
- ✓ Lökosit migrasyonu
- ✓ Adezyon moleküllerinin salınımı
- ✓ Nötrofil akivasyonu
- ✓ Akut faz reaktanlarının indüksiyon

Tbc gibi granülomatoz enfeksiyonlar
Hücre içi patojenler (listeria, salmonella)
Virüsler (HBV, VZV, JCV)
İnvaziv fungal enfeksiyonlar (nötropeni)

Ali T et al. Drug Healthc Patient Saf 2013;5:79e99.
Rheumatology 2018;57:2096-2100

TNF alfa inhibitörleri

- **Ciddi enfeksiyonlar ilk 3-6 ayda görülür.**
- **Tekrarlayan CE sık, indeks enfeksiyon sonrası yıllık tekrarlama oranın % 26'dır.**
- **CMV ve EBV reaktivasyonu bildirilmiş fakat sayı azdır.**
- **HZ ile ilgili farklı çalışmalarda çelişen sonuçlar mevcut (30 binden fazla hastanın dahil olduğu en geniş ABD vaka serisinde risk artışı bildirilmezken, Avrupa kayıtları HZ riskinde 2 kat artış bildirmiş).**
- **HCV reaktivasyonu nadir de olsa bildirilmiş.**

Rheumatology 2018;57:2096-2100

Winthrop KL et al. JAMA 2013

RHEUMATOLOGY

Rheumatology 2018;57:vii5–vii10
doi:10.1093/rheumatology/key059

20 years of ex
inhibitors: wh

Ciddi enfeksiyon görülme sıklığı çalışmalarda benzer.

En sık cilt enfeksiyonları ve alt solunum yolları infeksiyonu görülmekte, RA hastalarında pnömoni nedeni ile hastaneye yatış TNF alfa kullanımından bağımsız.

Enfeksiyon risk faktörlerinin; biyolojik ilaca başlama yaşı, ESR değeri ve beraberinde yüksek doz steroid kullanımı

DMARDs approved for the treatment of active RA in mid-1990s. They still

Aktif tüberküloza duyarlılık ve LTBE hastalarda reaktivasyon riskinde artış.

Tedaviye başlamadan önce aktif tüberküloz ve LTBE reaktivasyonu açısından tarama yapılmalıdır.

verse events. Effectiveness analysed from drug registries and safety issues are

Tüm hastalar Hepatit B için taranmalıdır.

ong-term experience, rheumatoid arthritis, safety, TNF inhibitors

ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an infectious diseases perspective (Soluble immune effector molecules [II]: agents targeting interleukins, immunoglobulins and complement factors).

Winthrop KL[1], Mariette X[2], Silva JT[3], Benamu E[4], Calabrese LH[5], Dumusc A[6], Smolen JS[7], Aguado JM[8], Fernández-Ruiz M[8].

Author information

Solubl immun efektör moleküler:

- ✓ **İnterlökinler**
- ✓ **İmmunglobulinler**
- ✓ **Kompleman faktörler**

Abstract

BACKGROUND: The present r GICH) Consensus Document on the safety of targ

AIMS: To review, from an Infect noglobulins and complement factors and to sug

SOURCES: Computer-based M

CONTENT: Patients receiving i (mepolizumab) agents have a moderate risk of infection and targeted agents (tocilizumab and siltuximab) is associated with a risk increase similar to that observed with anti-tumour necrosis factor-α agents. IL-12/23-targeted agents (ustekinumab) do not seem to pose a meaningful risk of infection, although screening for latent tuberculosis infection may be considered and antiviral prophylaxis should be given to hepatitis B surface antigen-positive patients. Therapy with IL-17-targeted agents (secukinumab, brodalumab and ixekizumab) may result in the development of mild-to-moderate mucocutaneous candidiasis. Pre-treatment screening for Strongyloides stercoralis and other geohelminths should be considered in patients who come from areas where these are endemic who are receiving IgE-targeted agents (omalizumab). C5-targeted agents (eculizumab) are associated with a markedly increased risk of infection due to encapsulated bacteria, particularly Neisseria spp. Meningococcal vaccination and chemoprophylaxis must be administered 2-4 weeks before initiating eculizumab. Patients with high-risk behaviours and their partners should also be screened for gonococcal infection.

IMPLICATIONS: Preventive strategies are particularly encouraged to minimize the occurrence of neisserial infection associated with eculizumab.

IL-1 antagonistleri
(Anakinra, Canakinumab, Gevokizumab, Rilonacept)

IL-1 ailesi immün sistemin anahtar komponenti

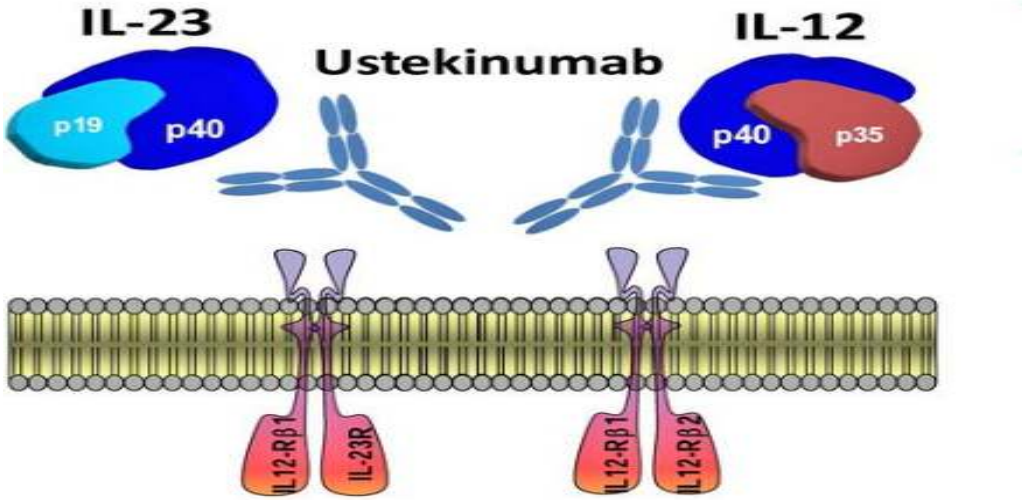
✓<u>VZV, HBV reaktivasyon riski yok</u>

✓Komorbiditesi olan, ileri yaş hastalarda ciddi enfeksiyon riskinde belirgin artış

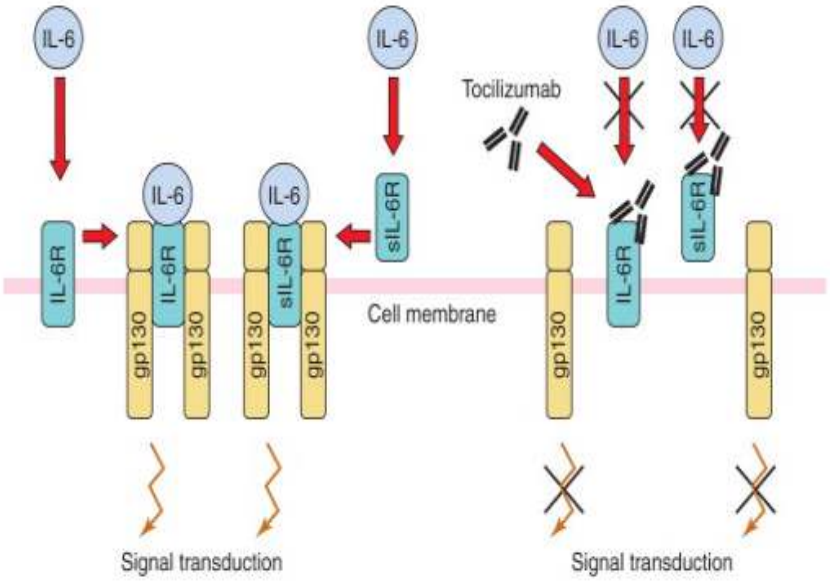
✓**<u>LTBE açısından tedavi öncesi tarama</u>**

IL-12/23 p40 antagonistleri (Usekinumab)

- ✓ LTBE açısından tedavi öncesi tarama
- ✓ HBV açısından tarama



IL-6 antagonistleri: (Tocilizumab)



- IL-6’ nın hem membrana bağlı hem de soluble formu ile yarışmaya girer
- Böylece doğal sitokin IL-6’ nı reseptörüne bağlanmasını engeller, sinyal iletimini durdurur

IL-6 antagonistleri (Tocilizumab)

✓ IL-6 gibi akut faz yanıtı oluşumunda çok önemli olan sitokinin aktivitesini bloke ettiği için, bu tedavi ile CRP düzeyleri hızla düşmektedir.

✓ Bu ilacı kullanan hastalarda gelişen enfeksiyonlarda ateş ve CRP yüksekliği gibi uyarıcı bulgular görülmeyebilir.

✓ **Anti-TNF ajanlara benzer artmış enfeksiyon riski!!!!**

✓ **Benzer koruma stratejisi**

Clin Microbiol Infect. 2018 Jun;24 Suppl 2:S53-S70. doi: 10.1016/j.cmi.2018.02.009. Epub 2018 Feb 16.

ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an infectious diseases perspective (Intracellular signaling pathways: tyrosine kinase and mTOR inhibitors).

Reinwald M[1], Silva JT[2], Mueller NJ[3], Fortún J[4], Garzoni C[5], de Fijter JW[6], Fernández-Ruiz M[7], Grossi P[8], Aguado JM[7].

Author information

Abstract

BACKGROUND: The pr...es (ESCMID) Study Group for Infections in Compro...pies.

AIMS: To review, from a...ular signaling pathways and to suggest preventi...

SOURCES: Computer-b...

CONTENT: Although BC...as been associated with cytomegalovirus and he...susceptibility. The effect of Bruton tyrosine kinase inhibitors (ibrutinib) among patients with B-cell malignancies is difficult to distinguish from that of previous immunosuppression. However, cases of Pneumocystis jirovecii pneumonia (PCP), invasive fungal infection and progressive multifocal leukoencephalopathy have been occasionally reported. Because phosphatidylinositol-3-kinase inhibitors (idelalisib) may predispose to opportunistic infections, anti-Pneumocystis prophylaxis and prevention strategies for cytomegalovirus are recommended. No increased rates of infection have been observed with venetoclax (antiapoptotic protein Bcl-2 inhibitor). Therapy with Janus kinase inhibitors markedly increases the incidence of infection. Pretreatment screening for chronic hepatitis B virus and latent tuberculosis infection must be performed, and anti-Pneumocystis prophylaxis should be considered for patients with additional risk factors. Cancer patients receiving mTOR inhibitors face an increased incidence of overall infection, especially those with additional risk factors (prior therapies or delayed wound healing).

IMPLICATIONS: Specific preventive approaches are warranted in view of the increased risk of infection associated with some of the reviewed agents.

Hücre içi sinyal yolları üzerine etkili ajanlar:

- ✓ **Tirozin kinaz inhibitörleri**
- ✓ **mTOR inhibitörleri**
- ✓ **JAK/STAT inhibitörleri**

JAK/STAT inhibitörleri

Tofacitinib

Barnicitinib

mTOR inhibitörleri

Sirolomus

Everolimus

mTOR inhibitörleri
JAK/STAT inhibitörleri

Agents	Increased risk of overall infection	Risk of OI	Risk of PCP	Risk of HBV reactivation	Observations and recommendations
Ruxolitinib, tofacitinib, baricitinib	Major	PCP, HZ, tuberculosis, CMV, EBV, PML	Yes (particularly in presence of additional risk factors)	Yes	• Increased risk of overall infection and OIs • Screening for chronic HBV infection before starting therapy • Antiviral prophylaxis while on therapy in HBsAg-positive patients • Monitoring for HBV viral load in anti-HBc positive, HBsAg-negative patients to assess eventual reactivation of occult HBV infection • Screening for LTBI before starting treatment (followed by appropriate therapy if needed)
Sirolimus, everolimus temsirolimus,	Major	HZ, tuberculosis	No	Yes	• Increased risk of infection in cancer patients, especially in those with additional risk factors (i.e., RCC, prior or concomitant cancer therapies, delay in wound healing or aphthous stomatitis). • Screening for chronic HBV infection and LTBI before starting therapy (followed by appropriate therapy if needed) • No expected benefit from the universal use of antibacterial, antiviral or anti-*Pneumocystis* prophylaxis

LTBE ve HBV açısından tedavi öncesi tarama yapılmalıdır.

Clinical Microbiology and Infection (2018)

Clin Microbiol Infect. 2018 Jun;24 Suppl 2:S71-S82. doi: 10.1016/j.cmi.2018.02.003. Epub 2018 Feb 12.

ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an infectious diseases perspective (Agents targeting lymphoid cells surface antigens [I]: CD19, CD20 and CD52).

Mikulska M[1], Lanini S[2], Gudiol C[3], Drgona L[4], Ippolito G[2], Fernández-Ruiz M[5], Salzberger B[6].

⊕ Author information

Abstract

BACKGROUND: The present review is part of the ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and bio

AIMS: To review, from an Infectious Disease CD19, CD20 and CD52 and to suggest preventive recommendations.

SOURCES: Computer-based MEDLINE sea therapeutic family.

CONTENT: Although CD19-targeted agents (blinatumomab or inebilizumab) are not associated with an increased risk of infection, they may cause IgG hypogammaglobulinaemia and neutropenia. The requirement for prolonged intravenous infusion of blinatumomab may increase the risk of catheter-associated bloodstream infections. Infection remains the most common non-haematological adverse effect of anti-CD20 monoclonal antibodies, including severe respiratory tract infection, hepatitis B virus (HBV) reactivation and varicella-zoster virus infection. Screening for chronic or resolved HBV infection is recommended for patients receiving anti-CD20 monoclonal antibodies. Antiviral prophylaxis should be offered for 12-18 months to hepatitis B surface antigen (HBsAg)-positive and HBsAg-negative/anti-hepatitis B core antibody (HBc)-positive patients. Anti-Pneumocystis prophylaxis should be considered in patients receiving concomitant chemotherapy, particularly steroids. Alemtuzumab (anti-CD52) increases the risk of infections, in particular among leukaemia and solid organ transplant patients. These populations benefit from anti-Pneumocystis prophylaxis, prevention strategies for cytomegalovirus infection, and screening for HBV, hepatitis C virus and tuberculosis. Antiviral prophylaxis for at least 6-12 months should be provided for HBsAg-positive patients.

IMPLICATIONS: As there are limited clinical data for many of the reviewed agents, special attention must be given to promptly detect and report emerging infectious complications.

CD 20 antagonistleri:

✓ Rituximab

CD 20 antagonistleri

(Rituximab, 90 Yibritumomab, Ofatumumab, Obinutuzumab, Ocrelizumab)

HBV reaktivasyonuna dikkat

Rituximab içeren rejimlerde reaktivasyon riski 6 kat fazla

HBsAg (-) / anti-HBc (+)

Aylık HBV DNA takibi

Preemptif antiviral tedavi

Daha pahalı
Uyum problemi

Clinical Microbiology and Infection (2018)

CD 20 antagonistleri

Rituximab vs PCP riski

Prednizolon (≥ 20 mg/gün en az 4 hafta) ile kombine edildiğinde PCP proflaksisi önerilmekte

ECİL-5'de de alemtuzumab, rituximab başta olmak üzere birçok DMARD için önerilmekte

Clinical Microbiology and Infection (2018)

ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an infectious diseases perspective (Immune checkpoint inhibitors, cell adhesion inhibitors, sphingosine-1-phosphate receptor modulators and proteasome inhibitors).

Redelman-Sidi G[1], Michielin O[2], Cervera C[3], Ribi C[4], Aguado JM[5], Fernández-Ruiz M[5], Manuel O[6].

Author information

Abstract

BACKGROUND: The present review is part of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Infections in Compromised Hosts (ESGICH) consens iological therapies.

AIMS: To review, from an infectious diseases perspectiv hibitors, LFA-3-targeted agents, cell adhesion inhibitors, sphingosine-1-phosphate receptor m suggest preventive recommendations.

SOURCES: Computer-based Medline searches with MeSH terms pertaining to each agent or therapeutic family.

CONTENT: T-lymphocyte-associated antigen 4 (CTLA-4) and programmed death (PD)-1/PD-1 ligand 1 (PD-L1)-targeted agents do not appear to intrinsically increase the risk of infection but can induce immune-related adverse effects requiring additional immunosuppression. Although $CD4^+$ T-cell lymphopenia is associated with alefacept, no opportunistic infections have been observed. Progressive multifocal leukoencephalopathy (PML) may occur during therapy with natalizumab (anti-α4-integrin monoclonal antibody (mAb)) and efalizumab (anti-CD11a mAb), but no cases have been reported to date with vedolizumab (anti-α4β7 mAb). In patients at high risk for PML (positive anti-JC polyomavirus serology with serum antibody index >1.5 and duration of therapy ≥48 months), the benefit-risk ratio of continuing natalizumab should be carefully considered. Fingolimod induces profound peripheral blood lymphopenia and increases the risk of varicella zoster virus (VZV) infection. Prophylaxis with (val)acyclovir and VZV vaccination should be considered. Proteasome inhibitors also increase the risk of VZV infection, and antiviral prophylaxis with (val)acyclovir is recommended. Anti-Pneumocystis prophylaxis may be considered in myeloma multiple patients with additional risk factors (i.e. high-dose corticosteroids).

IMPLICATIONS: Clinicians should be aware of the risk of immune-related adverse effects and PML in patients receiving immune checkpoint and cell adhesion inhibitors respectively.

CTLA-4 inhibitörleri

✓ Abatacept

Abatasept

- CTLA4-IgG1
- Rekombinant füzyon proteinidir
- T hücre aktivasyonunu önler
- Latent TB reaktivasyonu nedeni ile tarama
- Tedavi öncesi HBV taranmalıdır.

Neyin Altına İmza Atıyoruz?

- Hastada halen klinik olarak aktif tüberküloz veya malignite bulunmamaktadır.
- Hasta, fungal enfeksiyon gelişimi riski yönünden değerlendirilmiştir.
- Hasta, ilacın tüberküloz, lenfoma ve malignite dahil riskleri konusunda uyarılmıştır.
- Bu formda yer alan ilaçların uygulanması için uygun aşıların yapılması önerilmiştir.
- Tosilizumab tedavisi alacak hastalar, komplike divertiküllit belirtisi olabilecek karın ağrısı gibi semptomlar açısından uyarılmıştır.
- ..... tedavisi almasında medikal sakınca yoktur.

.....	.....	.....
İmza Adı Soyadı (Kaşe) Reçete Eden Hekim	İmza Adı Soyadı (Kaşe) İç Hastalıkları Uzmanı veya Çocuk Hastalıkları Uzmanı	İmza Adı Soyadı (Kaşe) Göğüs Hastalıkları Uzmanı veya Enfeksiyon Hastalıkları Uzmanı

* Bu form etanersept, infliksimab, adalimumab, abatasept, kanakinumab, ustekinumab, golimumab, tosilizumab, sertolizumab ve sekukinumab içeren ilaçlar için kullanılmaktadır.
* Bu form, tedavi süresince üç ayda bir doldurulmalıdır.
* Hasta başlangıçta ve ilaç kullanıldığı sürece tüberküloz, fungal enfeksiyon, lenfoma ve malign hastalıkların gelişimi yönünden reçete eden hekimler ile göğüs hastalıkları (veya enfeksiyon hastalıkları) ve iç hastalıkları (çocuklar için çocuk hastalıkları) uzmanlarınca yakından izlenmelidir.

- **Öykü**

–Özgeçmiş

–Soygeçmiş

  - **–Tüberküloz öyküsü**
  - **– Aşı öyküsü sorgulanması**

- **Fizik muayene**
- **Yapılacak tetkikler**
  - –PA akciğer grafisi
  - –PPD veya IGRA testleri
  - –HBsAg, anti-HBc,anti-HBs
  - –Anti-HCV
  - –Anti-HIV
  - –Anti-HAV IgG
  - –KKK, Suçiçeği
  - –CMV? PJP? JCV?

RHEUMATOLOGY
Guidelines
British Society for Rheumatology
Rheumatology 2019;58:220–226
doi:10.1093/rheumatology/key207
Advance Access publication 21 August 2018

The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis—Executive summary

Mycobacterium tuberculosis: screening for TB before starting a biologic

(i) All patients require screening for tuberculosis (TB) before starting a biologic (grade 1B, SOA 98%).
(ii) Screening for TB should include checking for previous TB exposure and treatment, perform a clinical examination, chest X-ray (CXR) and either a TST or IGRA or both, as appropriate (grade 2C, SOA 98%).
(iii) For patients on immunosuppressive therapy with a normal CXR, a TST is *not* helpful, as immunosuppression hinders interpretation (grade 2C, SOA 98%).
(iv) Patients with an abnormal CXR, previous history of TB or TB treatment should be referred to a specialist with an interest in TB prior to commencing a biologic (grade 2C, SOA 99%).
(v) Immunocompromised patients screened for latent TB with an IGRA alone or together with a TST and found to have a positive result in either test should be considered for treatment prior to starting biologic therapy (grade 2C, SOA 96%).

Latent and reactivated TB

(i) Patients should be treated with prophylactic anti-TB treatment prior to commencing a biologic (grade 1B, SOA 99%); therapy may be commenced after completing at least 1 month of anti-TB treatment and patients should be monitored every 3 months (grade 2C, SOA 91%).
(ii) Patients who have had previous inadequate treatment for active TB should be investigated for active TB. In these individuals even when active disease has been excluded, the annual risk of TB (reactivation) is much higher than the general population rate, so the risk-benefit analysis favours chemoprophylaxis (grade 1C, SOA 98%).
(iii) As TB reactivation risk is higher with anti-TNF mAb drugs (notably ADA and IFX) than for ETN, consider ETN in preference for those who require anti-TNF therapy and are at high risk of TB reactivation (grade 1B, SOA 99%).

Rheumatology 2019; 58: 220-226.

RHEUMATOLOGY

Guidelines

British Society for Rheumatology

Rheumatology 2019;58:220–226
doi:10.1093/rheumatology/key207
Advance Access publication 21 August 2018

The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis—Executive summary

Active TB

(i) Patients with evidence of active TB should be treated before starting a biologic (grade 1C, SOA 99%); therapy may be commenced after completing at least 3 months of anti-TB treatment, and there is evidence that the patient is improving with evidence of culture negativity (grade 2C, SOA 91%).

HIV

(i) Risk factors for HIV infection should be documented prior to commencing a biologic and, if present, an HIV test should be performed (grade 2C, SOA 97%).

(ii) If considering the use of biologic therapy in HIV positive patients, this should be discussed with an HIV specialist. It should be borne in mind that a reasonable benefit–risk ratio for HIV patients exists with anti-TNF therapy if HIV infection is controlled ($CD4^+$ count >200 cells/mm^3 and viral load undetectable) and anti-TNF is given in combination with highly active anti-retroviral therapy (grade 2C, SOA 99%).

Rheumatology 2019; 58: 220-226.

RHEUMATOLOGY

Guidelines

British Society for Rheumatology

Rheumatology 2019;58:220–226
doi:10.1093/rheumatology/key207
Advance Access publication 21 August 2018

The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis—Executive summary

HBV and HCV

(i) Patients should be screened for HBV and HCV infection (grade 1C, SOA 98%).

(ii) In patients who are HBV positive, a risk–benefit assessment should be undertaken, as biologics may be safe if appropriate anti-viral treatment is given, working closely with a hepatologist (grade 1C, SOA 99%).

(iii) Studies to date suggest that though biologic therapy does not appear to have a detrimental effect on HCV infection, it should continue to be used only with caution in such patients, following a risk–benefit decision made with a hepatologist (grade 1C, SOA 96%).

Rheumatology 2019; 58: 220226


illness
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contagious
patient
tuberculosis
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healthcare
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health
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respiration
care
bacteria
vaccination
organ
organism
breakdown
bronchus
antibiotics
bacterium
cough
infectious
cheek
unhealthy
vaccine
concept
cell
prevention
biology
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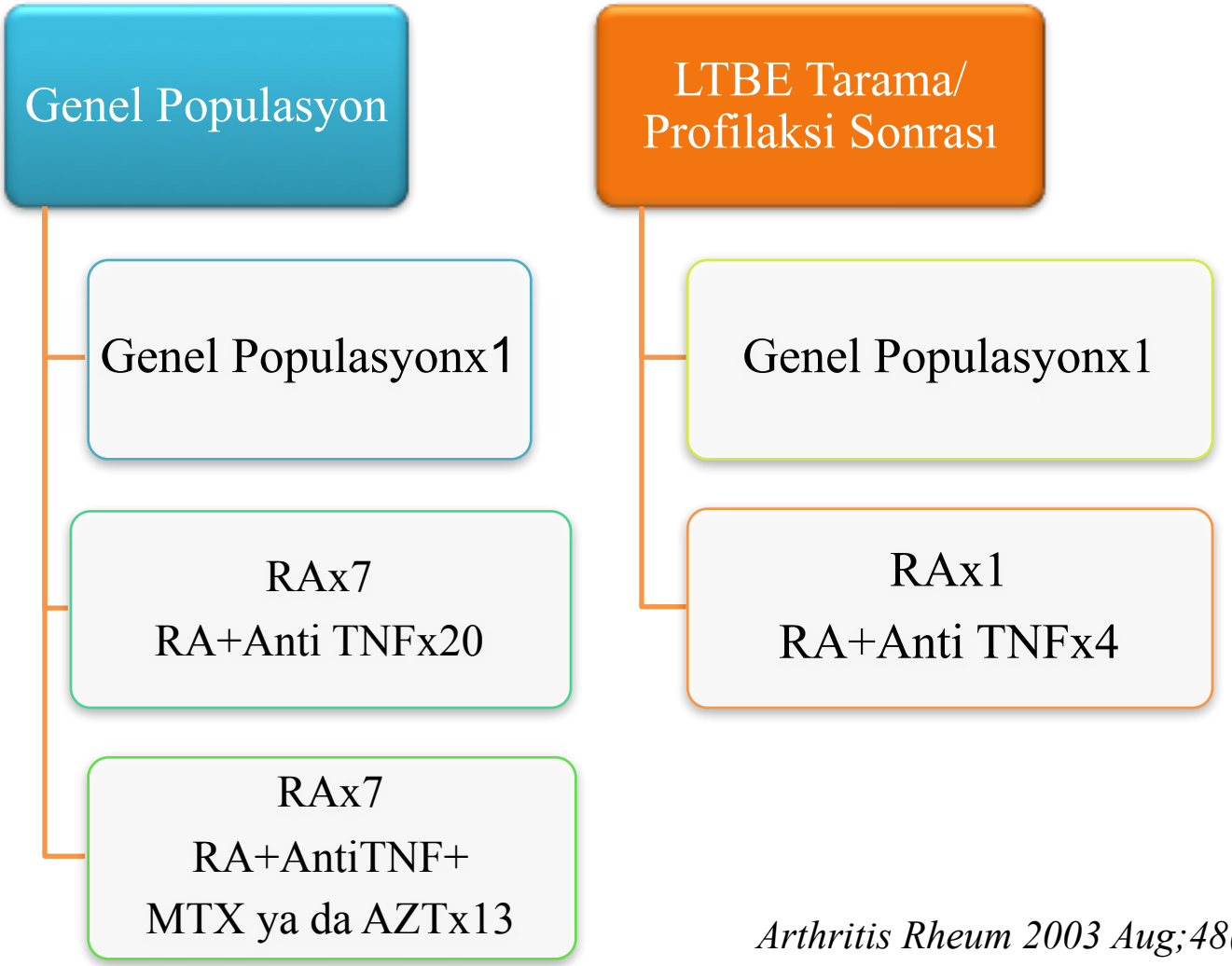
technology
system
sickness
sinusitis
blood
epidemic
test
medical
bronchitis
infection
deadly
mycobacterium
streptococci
medicine
breathing

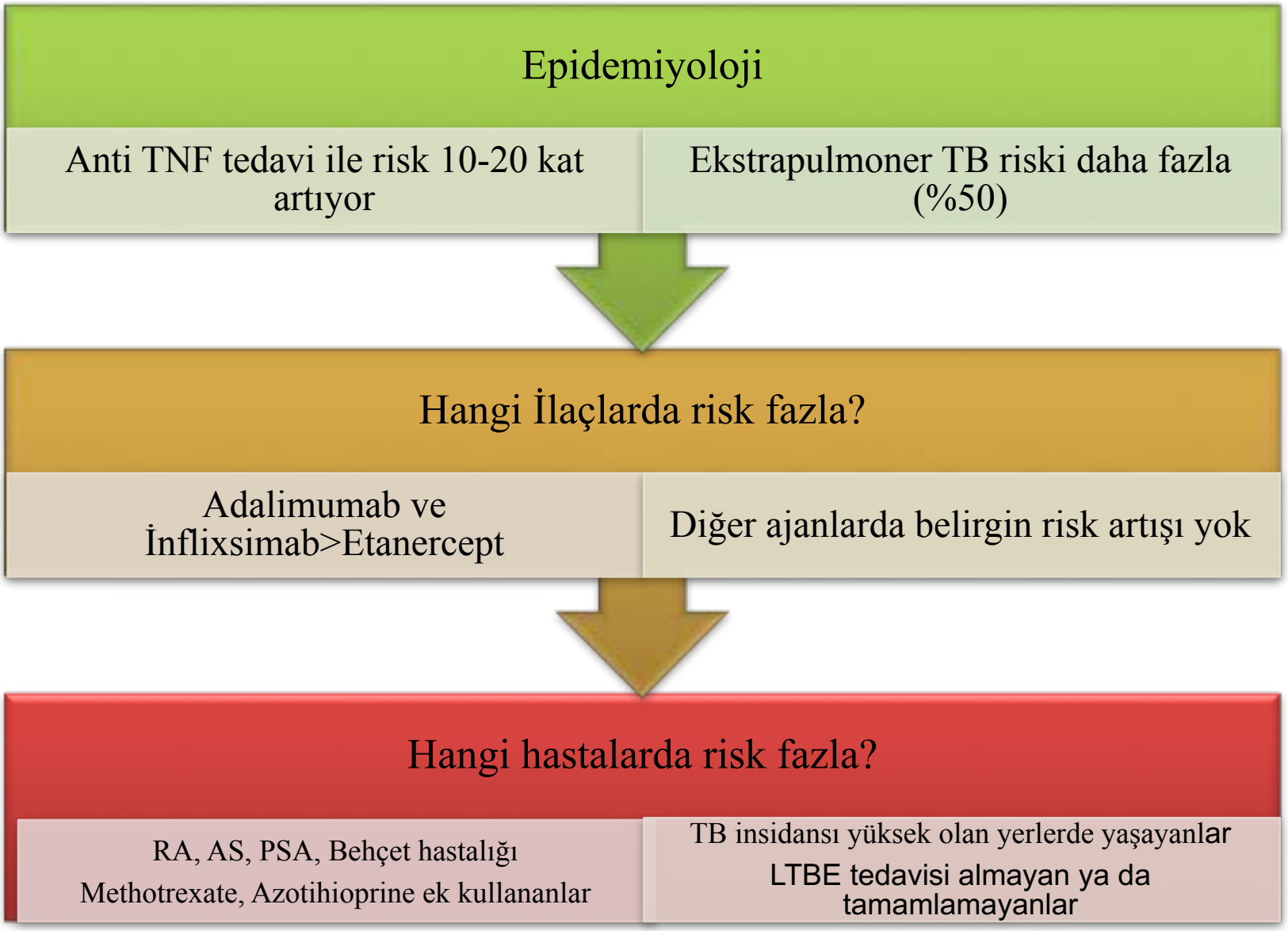
Biyolojik Ajanlar Tüberküloz Epidemiyoloji



Arthritis Rheum 2003 Aug;48(8):2122-7

Lorenzetti R et al. Ann Med 2014

Biyolojik Ajanlar Tüberküloz Epidemiyoloji



T.C. SAĞLIK BAKANLIĞI

TÜBERKÜLOZ TANI VE TEDAVİ REHBERİ

2. BASKI

Ankara - 2019

16.

ANTİ-TNF İLAÇ KULLANIMI VE TÜBERKÜLOZ

Türkiye'de TB insidansı 16/100 000

Anti-TNF kullananlarda risk Türkiye'de 10-20 kat fazla

TBC Açısından Nasıl Takip Edelim?

Akif TBC varlığında anti-TNF tedavisi kontrendike, bu nedenle hastalar tedavi öncesi araştırılmalıdır.

Anti-TNF tedavisi kesildikten sonra da TBC riski devam edebilir, en az 6 ay takip edilmelidir.

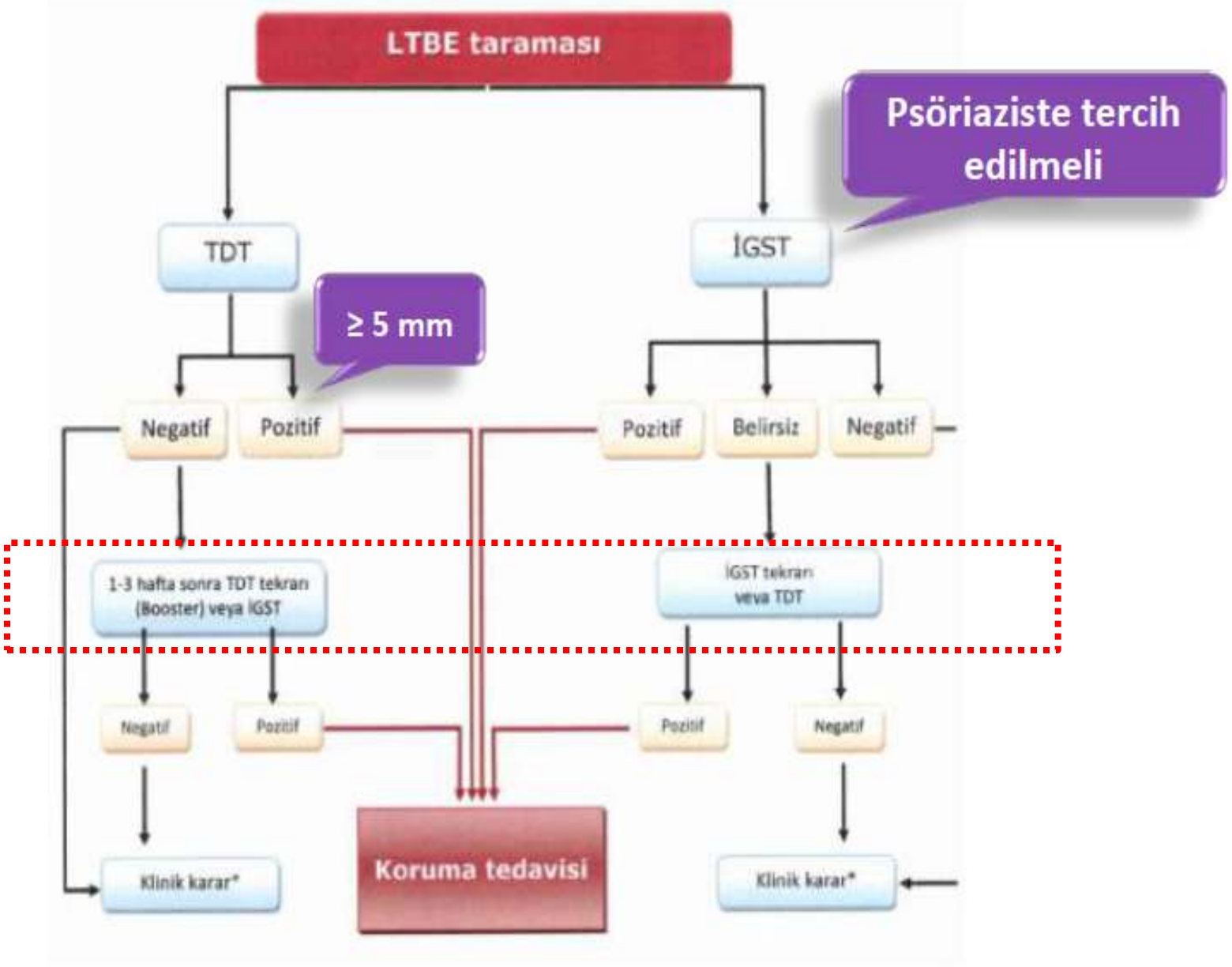
TBC tanısı konulan hastalarda tedavi tamamlanmadan anti-TNF tedavi başlanmamalıdır. (Kar-zarar hesabı yapılarak istisnai durumlar hariç)

Anti-TNF başlanan hastalar asemptomatik olsalar bile TBC açısından (anamnez, FM, radyoloji) 6 ayda bir kontrol edilmelidir.

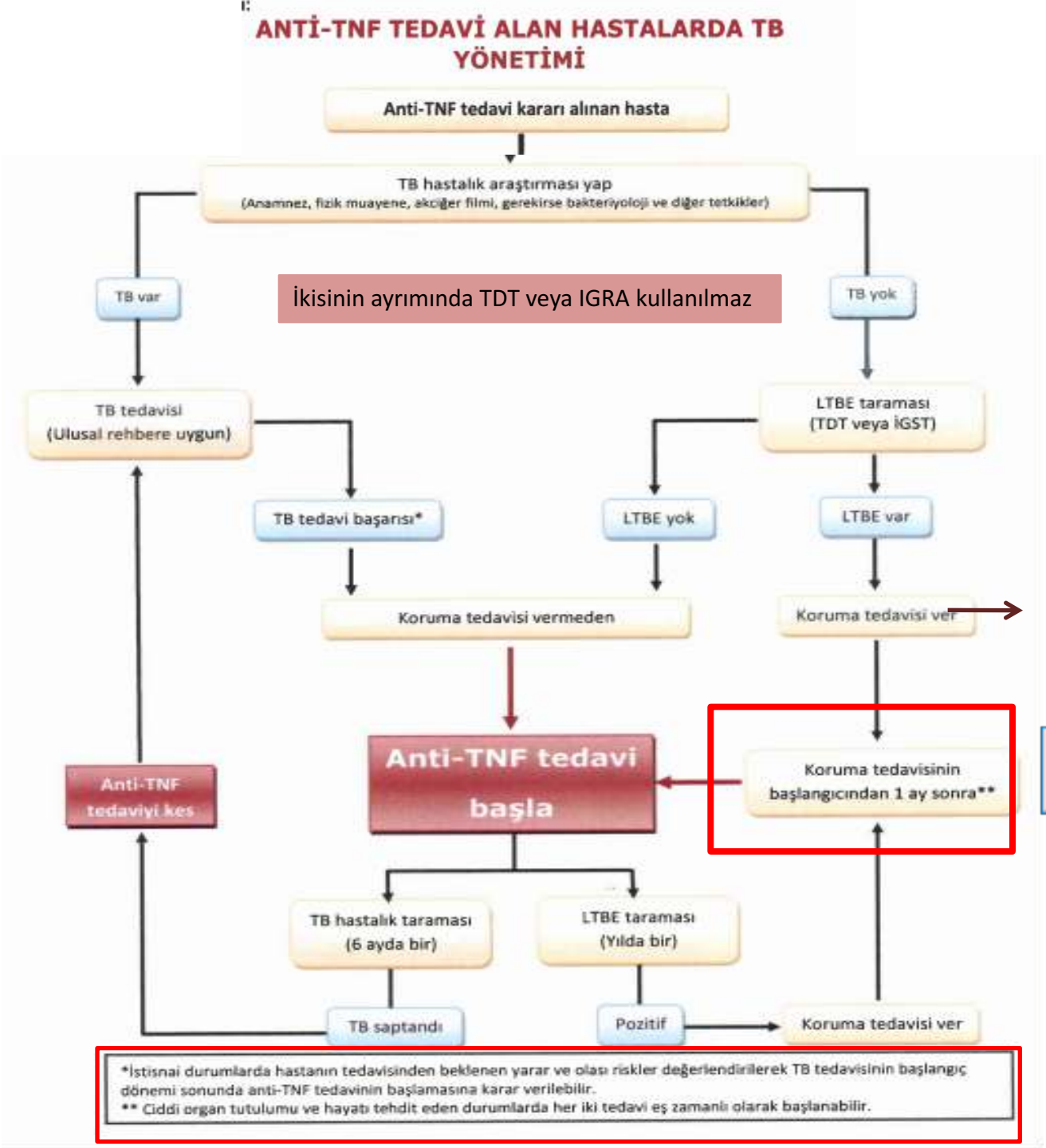
Biyolojik Ajan ve LTBI Hangi Test?

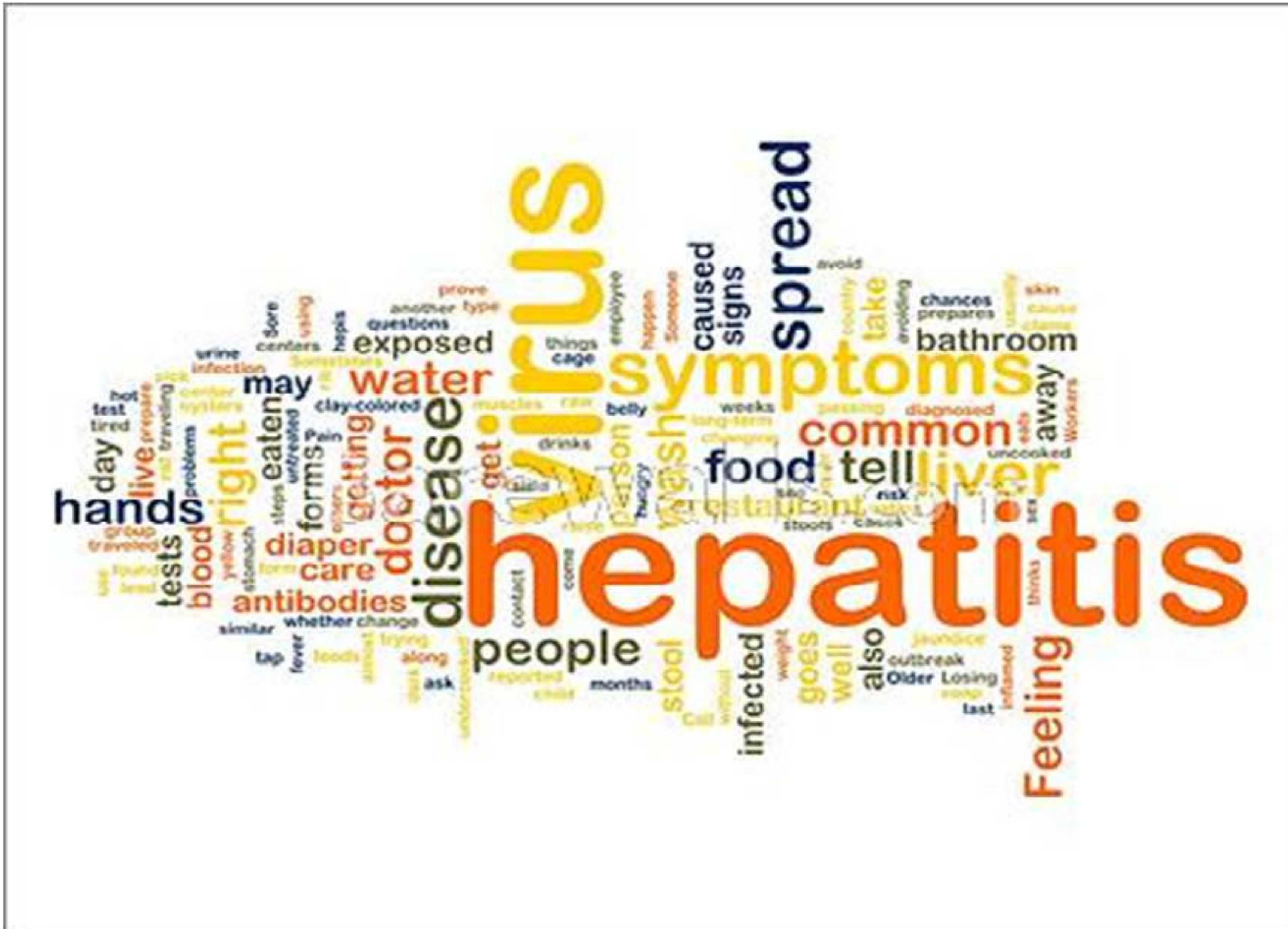
PPD ve Yeni Tanı Testleri Özellikleri	PPD	IFN'a dayalı testler
BCG	Etkilenir	Etkilenmez
Nontüberküloz mikobakteri (NTM)	Etkilenir	Etkilenmez
Duyarlılık	%75-90	%80-95
Özgüllük	%70-95	%95-100
BCG'li Özgüllük	%53	%89
Test Pozitif TB gelişme ilişkisi	Orta	Güçlü
Booster Etki	Var	Yok
TB Hast. Şiddeti	Etkilenme Az	Etkilenmeyebilir
TB Temas İlişkisi	Var	Var
İmmünsupresyon	Etkiler	Etkilenme Az
Ağır deri lezyonları	Etkilenebilir	Etkilenmez
Aktif TB Öngörü	Var	Daha Güçlü
Test Süresi	2-3 gün	1-2 Gün
Maliyet	Ucuz	Pahalı
Personel İhtiyacı	Var	Var
Cihaz Gereksinim	Yok	Var

PPD sonucu hem immünsüpresyondan hem deri lezyonlarından etkilenir ve latent TB'un profilaksisi için yanlış karar verdirebilir.


LTBE taraması
Psöriaziste tercih edilmeli
TDT
İGST
≥ 5 mm
Negatif
Pozitif
Pozitif
Belirsiz
Negatif
1-3 hafta sonra TDT tekrarı (Booster) veya İGST
İGST tekrarı veya TDT
Negatif
Pozitif
Pozitif
Negatif
Klinik karar*
Koruma tedavisi
Klinik karar*

ANTİ-TNF TEDAVİ ALAN HASTALARDA TB YÖNETİMİ




hepatitis
virus
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people
common
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Older
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VIRUS ALERT
HBV
VIRUS ALERT

Gastroenterology 2017;152:1297–1309

REVIEWS IN BASIC AND CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

HEPATOLOGY

AASLD

PRACTICE GUIDANCE | HEPATOLOGY, VOL. 67, NO. 4, 2018

Update on Prevention, Diagnosis, and Treatment of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance

Norah A. Terrault,[1] Anna S.F. Lok,[2] Brian J. McMahon,[3] Kyong-Mi Chang,[4] Jessica P. Hwang,[5] Maureen M. Jonas,[6] Robert S. Brown Jr.,[7] Natalie H. Bzowej,[8] and John B. Wong[9]

REVIEW

Immunosuppressive therapy and the risk of hepatitis B reactivation: Consensus report

Bilgehan Aygen[1], Ahmet Muzaffer Demir[2], Mahmut Gümüş[3], Oğuz Karabay[4], Sabahattin Kaymakoğlu[5], Aydın Şeref Köksal[6], İftihar Köksal[7], Necati Örmeci[1], Fehmi Tabak[8]

on the Prevention and Treatment of Hepatitis B Virus Reactivation During Immunosuppressive Drug Therapy

HBV Reaktivasyonu

Hbs Ag pozitif hastalarda

- HBV DNA negatif-pozitifleşme
- HBV DNA pozitif bazale göre ≥1 log10 artı
- ALT'de bazal değerin ≥3 katı artış veya ≥100IU/ml olması
- -HBV DNA'da artış ile birlikte

HBs Ag (-) Anti HBc (+) hastalarda

- ıBsAg pozitifleşme (HBsAg seroreversiyonu)
- HBsAg negatif ancak HBV DNA pozitifleşme

Klinik
- Subklinik form şiddetli/fatal hepatit
- Tedaviye rağmen mortalite oranı: %4-60

Pattula V. World J Hepatol 2015

Tarama CDC, EASL, APASL ve AASLD tarafından önerilir

- **HBsAg, anti-HBc, anti-HBs taraması**

REVIEW

Immunosuppressive therapy and the risk of hepatitis B reactivation: Consensus report

Bilgehan Aygen[1], Ahmet Muzaffer Demir[2], Mahmut Gümüş[3], Oğuz Karabay[4], Sabahattin Kaymakoğlu[5], Aydın Şeref Köksal[6], İftihar Köksal[7], Necati Örmeci[1], Fehmi Tabak[9]

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Cite this article as: Aygen B, Demir AM, Gümüş M, et al. Immunosuppressive therapy and the risk of hepatitis B reactivation: Consensus report. Turk J Gastroenterol 2018; 29: 259-69.

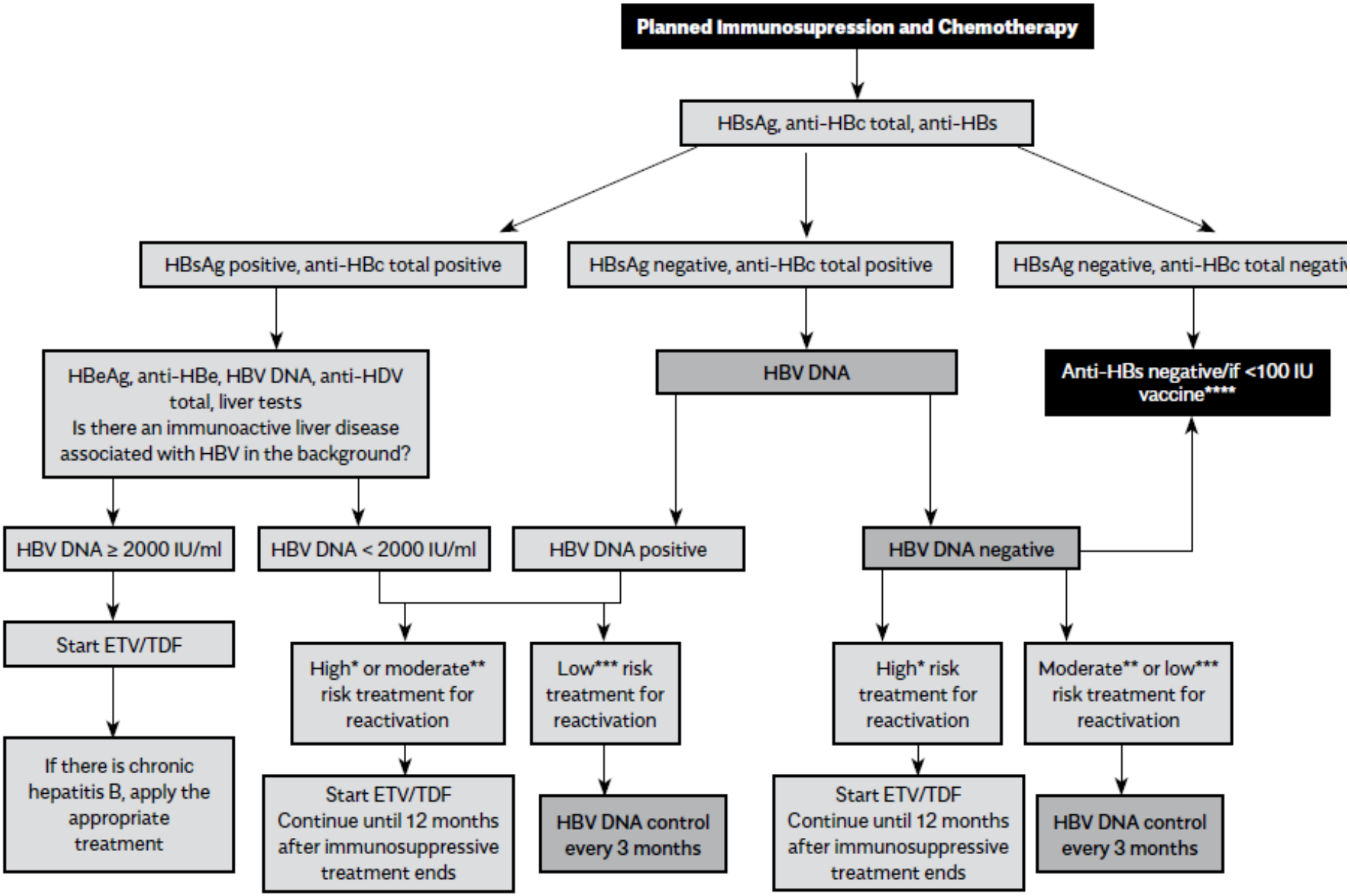
ABSTRACT

This consensus report includes expert opinions and recommendations regarding the screening, and if necessary, the follow-up, prophylaxis, and treatment of hepatitis B before the treatment in patients who will undergo immunosuppressive therapy due to an emergency risk of hepatitis B reactivation. To increase awareness regarding the risk of hepatitis B reactivation in immunosuppressive patients, academicians from several university health research and training centers across Turkey came together and discussed the importance of the subject, current status, and issues in accordance with the current literature data and presented solutions.

Keywords: Hepatitis B, immunosuppressive therapy, reactivation risk, antiviral prophylaxis

HBV reaktivasyon riski	İlaç grubu	İlaç
Yüksek (>10%)	B hücre suppresyonu Antrasikllin türevleri Kortikosteriodler	Rituximab Ofatumumab Doxorubicin Epirubicin (HBsAg-positive/anti-HBc-positive) ≥4 weeks, HBsAg-pozitif/anti-HBc-positif, moderate/high dose (10-20 mg/>20 mg)
Orta (1%-10%)	TNF-α inhibitorleri Other cytokine inhibitors and integrin inhibitors Tirozin kinase inhibitors Anthracycline derivatives Kortikosteriodler	Infliximab Etanercept Adalimumab Certolizumab Abatacept and Abatacept Ustekinumab Natalizumab Vedolizumab Imatinib Nilotinib Doxorubicin Epirubicin (HBsAg-negatif/anti-HBc-positif) ≥4 weeks, HBsAg-positive/anti-HBc-positive, low dose (<10mg) ≥4 weeks, HBsAg-negative/anti-HBc-positive, moderate/high dose (10-20 mg/>20 mg)
Düşük (<1)	Conventional immunosuppression Intra-articular corticosteroids Kortikosteriodler	Azathioprine 6-mercaptopurine Methotrexate ≤1 week ≥4 weeks, HBsAg-negative/anti-HBc-positive, low dose (<10mg)

J Gastroenterol 2018; 29: 259-69



J Gastroenterol 2018; 29: 259-69.


VIRUS ALERT
VIRUS ALERT

Hepatit C

Arthritis & Rheumatology 2016; 68(1):1-26.


vaccination
immune system
infectious disease
health
antibodies
virus
pathogen
infection
protection
tropical disease
pharmaceuticals
healthcare
physician
prevent
quarantine
travelling
public health
hepatitis
bacteria
flu
flu shot
HPV
pandemic
yellow fever
immunity
chicken pox
polio
malaria
symptom
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risk
public health
malaria
yellow fever
chicken pox
prevent
quarantine
safety
hepatitis


TÜRKİYE
EKMUD
2006
TÜRKİYE ENFEKSİYON HASTALIKLARI VE KLİNİK MİKROBİYOLOJİ UZMANLIK DERNEĞİ
ERİŞKİN BAĞIŞIKLAMA
REHBERİ
2019

TÜRKİYE EKMUD

2006

TÜRKİYE ENFEKSİYON HASTALIKLARI VE KLİNİK MİKROBİYOLOJİ UZMANLIK DERNEĞİ

ERİŞKİN BAĞIŞIKLAMA REHBERİ

2019

Genel İlker

Tedavi öncesi

- İnaktif aşılar 2 hafta önce
- Canlı aşılar 4 hafta önce

Tedavi esnasında

- İnaktif aşılarda yanıt düşük
- Canlı aşılar önerilmez

Tedavi sonrası

- Yüksek doz steroid-4 hafta
- Ertancept – 4 hafta
  Diğer TNF-3 ay
  Rituksimab- 6 ay
  Leflunomid-12 ay

Aşı	18-64 yaş	65 ≥ yaş
İnfluenza	Yılda 1 doz aşı	
Pnömokok [1,2]	1-2 doz aşı	1-2 doz aşı
Tetanoz, difteri (Td)[3]	Her 10 yılda bir rapel doz aşı	
Hepatit B	3 doz aşı (0,1,6. aylar) (biyolojik ajan veya orta-yüksek doz kortikosteroid alan yüksek riskli hastalarda seroloji durumuna göre yüksek doz aşı 0,1,2 ve 6. aylarda çift doz- uygulanabilir)	
Hepatit A	2 doz aşı (0,6. aylar)	
Suçiçeği/Herpes zoster[4]	*İmmünsupresyonu olan hastalarda ve gebelerde kontrendike- özel durumlarda uzman görüşü alınarak aşı uygulanabilir.	
Kızamık, kızamıkçık, kabakulak (KKK)[4]	*İmmünsupresyonu olan hastalarda ve gebelerde kontrendike- özel durumlarda uzman görüşü alınarak aşı uygulanabilir	
Meningokok (kuadrivalan konjuge meningokok aşısı)[2]	*En az 2 ay arayla 2 doz aşı. Risk devam ediyorsa 5 yılda bir tekrarlanabilir.	
Haemophilus influenzae tip B[2]	*1 doz	
Human papillomavirüs (HPV)[5]	2 veya 3 doz	

Recommendation

2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

1. The vaccination status and indications for further vaccination in patients with AIIRD should be

‘ Romatoloji team’ aşı durumları ve aşılama planı için yıllık değerlendirme hastalara açıklanması

2. The individualised vaccination programme should be explained to the patient by the rheumatology

Aşılama hastalığın stabil olduğu dönemde yapılmalıdır.

physician, the rheumatology team and the patient.

Aşılama planı immunsupresyondan önce yapılmalıdır (özellikle B hücre deplesyonu).

4. Vaccines should preferably be administered prior to planned immunosuppression, in particular B-cell

Canlı olmayan aşılar DMARDSs ve glukortikoid tedavisi alırken yapılabilir.

5. Non-live vaccines can be administered to patients with AIIRD during the use of glucocorticoids and

Canlı aşı planlarken dikkatli olunmalıdır.

6. Live-attenuated vaccines may be considered with caution in patients with AIIRD.

Furer V, et al. Ann Rheum Dis 2019;0:1–14.

Table 6. Vaccination of Persons With Chronic Inflammatory Diseases on Immunosuppressive Medications

Vaccine	Planned Immunosuppression		Low-level Immunosuppression[a]		High-level Immunosuppression[a]	
	Recommendation	Strength, Evidence Quality	Recommendation	Strength, Evidence Quality	Recommendation	Strength, Evidence Quality
Haemophilus influenzae b conjugate	U	Strong, moderate	U	Strong, low	U	Strong, low
Hepatitis A	U	Strong, moderate	U	Strong, low	U	Strong, low
Hepatitis B	U	Strong, moderate	U	Strong, low	U	Strong, low
Diphtheria toxoid, tetanus toxoid, acellular pertussis; tetanus toxoid, reduced diphtheria toxoid; tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis	U	Strong, moderate	U	Strong, low	U	Strong, low
Human papillomavirus	U: 11–26 y	Strong, moderate	U: 11–26 y	Strong, low	U: 11–26 y	Strong, very low
Influenza-inactivated (inactivated influenza vaccine)	U	Strong, moderate	U	Strong, moderate	U	Strong, moderate
Influenza-live attenuated (live attenuated influenza vaccine)	X	Weak, very low	X	Weak, very low	X	Weak, very low
Measles, mumps, and rubella–live	U[b]	Strong, moderate	X	Weak, very low	X	Weak, very low
Measles, mumps, and rubella–varicella-live	U[b]	Strong, low	X	Weak, very low	X	Strong, very low
Meningococcal conjugate	U	Strong, moderate	U	Strong, moderate	U	Strong, low
Pneumococcal conjugate (PCV13)	R[c]	Strong, moderate	U: <6 y R: ≥6 y[c]	Strong, low strong, very low	U: <6 y R: ≥6 y[c]	Strong, low strong, very low
Pneumococcal polysaccharide (PPSV23)	R: age ≥2 y	Strong, low	R: age ≥2 y	Strong, low	R: age ≥2 y	Strong, very low
Polio-inactivated (inactivated poliovirus vaccine)	U	Strong, moderate	U	Strong, moderate	U	Strong, low
Rotavirus–live	U	Strong, moderate	X	Weak, very low	X	Weak, very low
Varicella–live	U[b]	Strong, moderate	X[d]	Weak, very low	X	Strong, moderate
Zoster–live	R: age 50–59 y[e] U: age ≥60 y	Weak, low strong, low	R: age 50–59 y[e] U: age ≥60 y	Weak, very low Strong, very low	X	Weak, very low

IDSA. Vaccination of the Immunocompromised Host CID. 2014;58(3):e44-100

Recommendation

2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

Tetanoz aşısı toplumdaki hastalar gibi, B hücre delesyonu yapan ilaç pasif immunizasyon düşün

6. Vaccination against yellow fever should be generally avoided in patients with AIIRD

HBV ve HAV aşıları risk grubunda yapılmalıdır.

7. Patients with AIIRD, in particular patients with systemic lupus erythematosus, should receive

Herpes zoster yüksek riskli hastalara yapılmalıdır.

population

Sarı humma aşısından kaçınılmalıdır.

SLE olmak üzere bu hastalarda HPV aşısı genel populasyon önerileri geçerlidir.

9. Live-attenuated vaccines should be avoided during the first 6 months of life in newborns of mothers

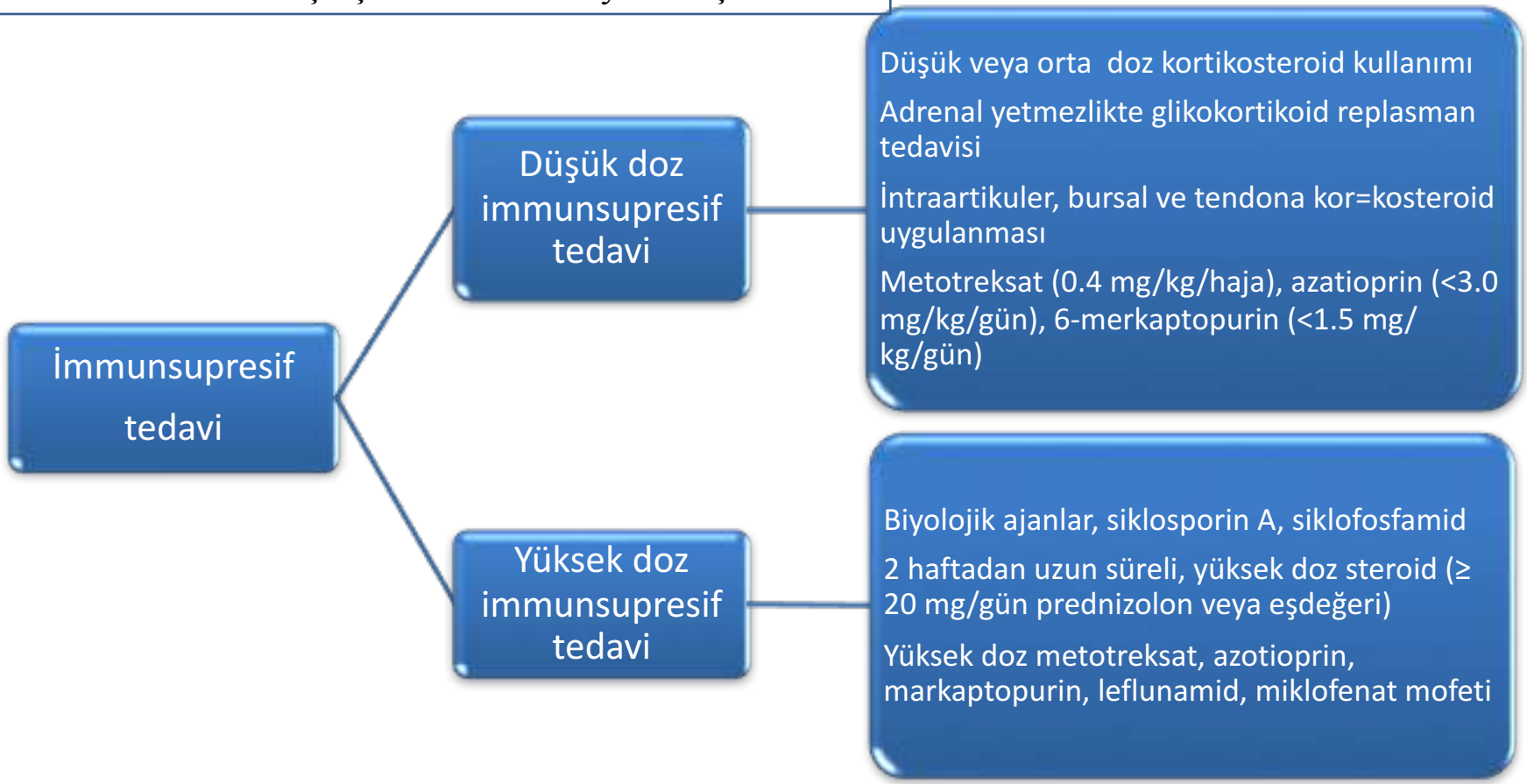
Hastanın aile bireyleri oral polio aşısı dışında ulusal kılavuzlara göre aşılanabilir.

Gebeliğinin ikinci yarısında biyolojik ilaç alan anne bebekleri ne ilk 6 ay canlı aşı yapılmamalıdır.

Furer V, et al. Ann Rheum Dis 2019;0:1–14.

Herpes zoster aşısı, düşük doz immunosupresif tedavi altında uygulanabilir !

Düşük dozda kullanılan birden çok immunosupresif ilaç birlikte etkisi canlı aşı için kontrendikasyon oluşturabilir !



Tanrıover MD, et al. Eur J Rhematol. 2016;3(1):29-35.

Table 2 Recommended Adult Immunization Schedule by Medical Condition and Other Indications United States, 2019

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 count <200	HIV infection CD4 count ≥200	Asplenia, complement deficiencies	End-stage renal disease, on hemodialysis	Heart or lung disease, alcoholism[1]	Chronic liver disease	Diabetes	Health care personnel[2]	Men who have sex with men
IIV or RIV	1 dose annually										
or										or	
LAIV	CONTRAINDICATED						PRECAUTION			1 dose annually	
Tdap or Td	1 dose Tdap each pregnancy	1 dose Tdap, then Td booster every 10 yrs									
MMR	CONTRAINDICATED	1 or 2 doses depending on indication									
VAR	CONTRAINDICATED	2 doses									
RZV *(preferred)*	DELAY				2 doses at age ≥50 yrs						
or					or						
ZVL	CONTRAINDICATED	1 dose at age ≥60 yrs									
HPV Female	DELAY	3 doses through age 26 yrs			2 or 3 doses through age 26 yrs						
HPV Male		3 doses through age 26 yrs			2 or 3 doses through age 21 yrs						2 or 3 doses through age 26 yrs
PCV13		1 dose									
PPSV23		1, 2, or 3 doses depending on age and indication									
HepA	2 or 3 doses depending on vaccine										
HepB	2 or 3 doses depending on vaccine										
MenACWY	1 or 2 doses depending on indication, then booster every 5 yrs if risk remains										
MenB	PRECAUTION	2 or 3 doses depending on vaccine and indication									
Hib		3 doses HSCT[3] recipients only			1 dose						

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

Precaution—vaccine might be indicated if benefit of protection outweighs risk of adverse reaction

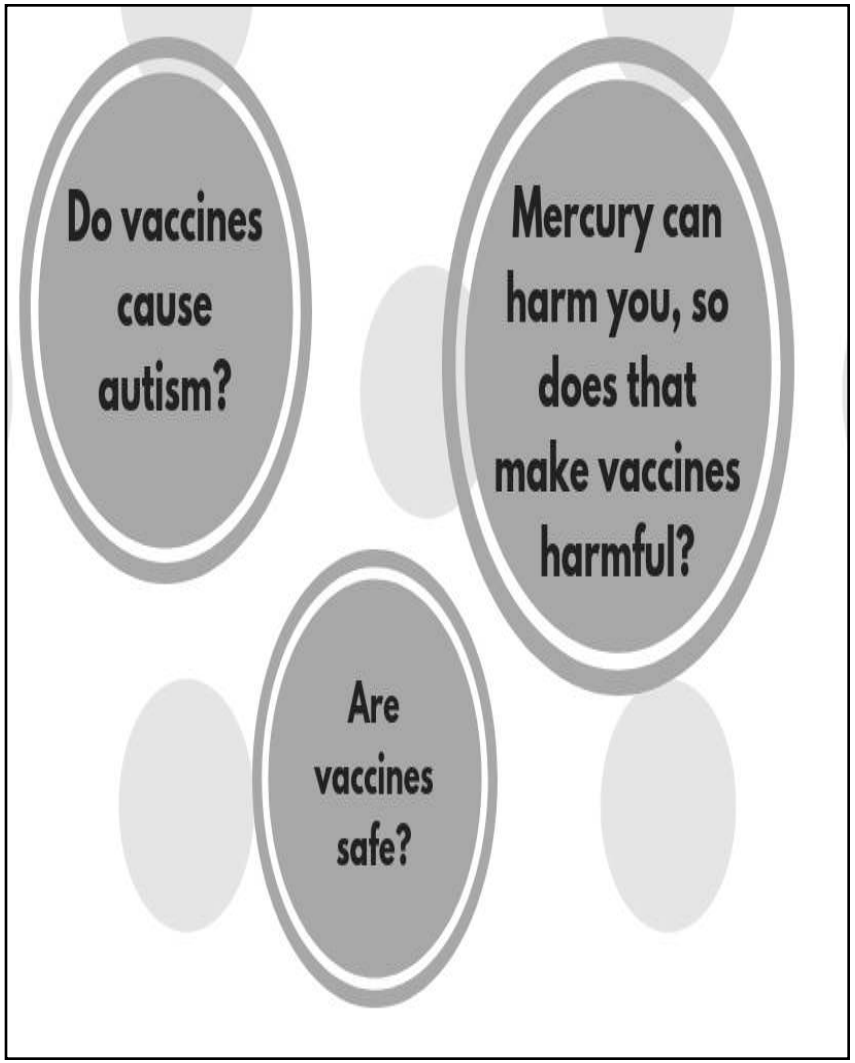
Delay vaccination until after pregnancy if vaccine is indicated

Contraindicated—vaccine should not be administered because of risk for serious adverse reaction

No recommendation

1. Precaution for LAIV does not apply to alcoholism. 2. See notes for influenza; hepatitis B; measles, mumps, and rubella; and varicella vaccinations. 3. Hematopoietic stem cell transplant.

Aşı-Otoimmünite İlişkisi?



✓Otoimmün hastalıklarda grip aşısına hastalıkta geçici alevlenme bazı olgu raporları olsa da prospektif çalışmalarda neden-sonuç ilişkisi gösterilememiş .

✓SLE ve RA'li hastalarda infeksiyondan daha fazla aktiviteye yol açmaz.

✓HBV aşısı SLE ve RA'li hastalarda hastalık aktivitesi üzerinde etkisi yok

✓KKK aşısı jüvenil idiopatik artritli hastalarda klinik veya laboratuvar olarak ölçülen bir kötüleşmeye yol açmamış .

Liao Z, et al.(2016. PLoS ONE 11(2): e0147856

THE TAKE-HOME MESSAGE

LTBE tarama

- TNF alfa inhibitörleri
- Abatasept
- Anakinra -Kanakinumab
- Tokilizumab
- Tofasitinib
- Ustekinumab
- Everelimus-Sirolimus

HBV tarama

- TNF alfa inhibitörleri
- Abatasept
- Anakinra-Kanakinumab
- Rituksimab
- Belimumab
- Tokilizumab
- Tofasitinib
- Ustekinumab
- Everelimus-Sirolimus

THE TAKE-HOME MESSAGE


MUTLU
SENELER
Yeni yılınız Kutlu Olsun