

Ensefalitlerde Akılcı Antiviral Kullanımı

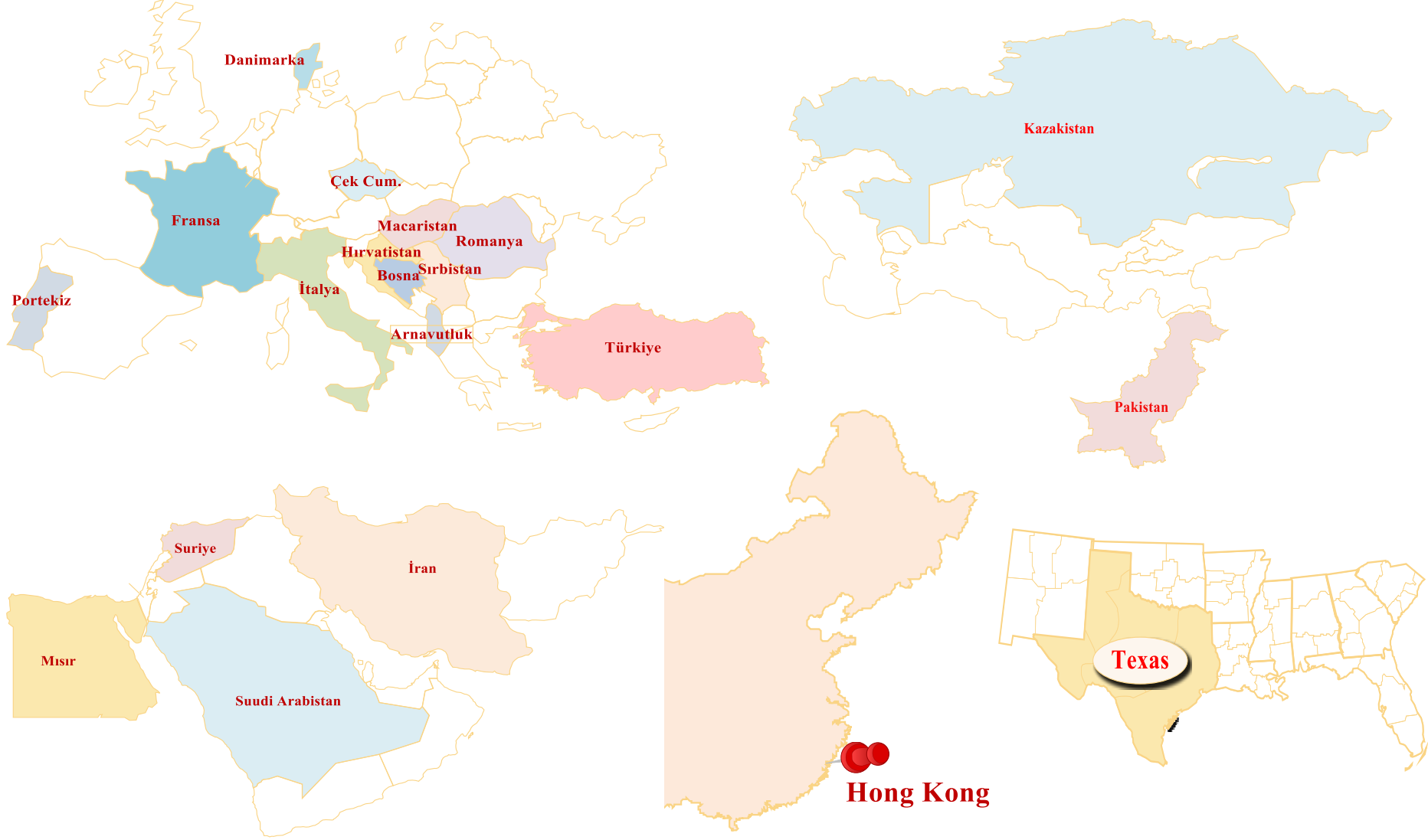


Prof. Dr. Hakan Erdem
GATA Enf.Hast ve Kl.Mik.A.D.



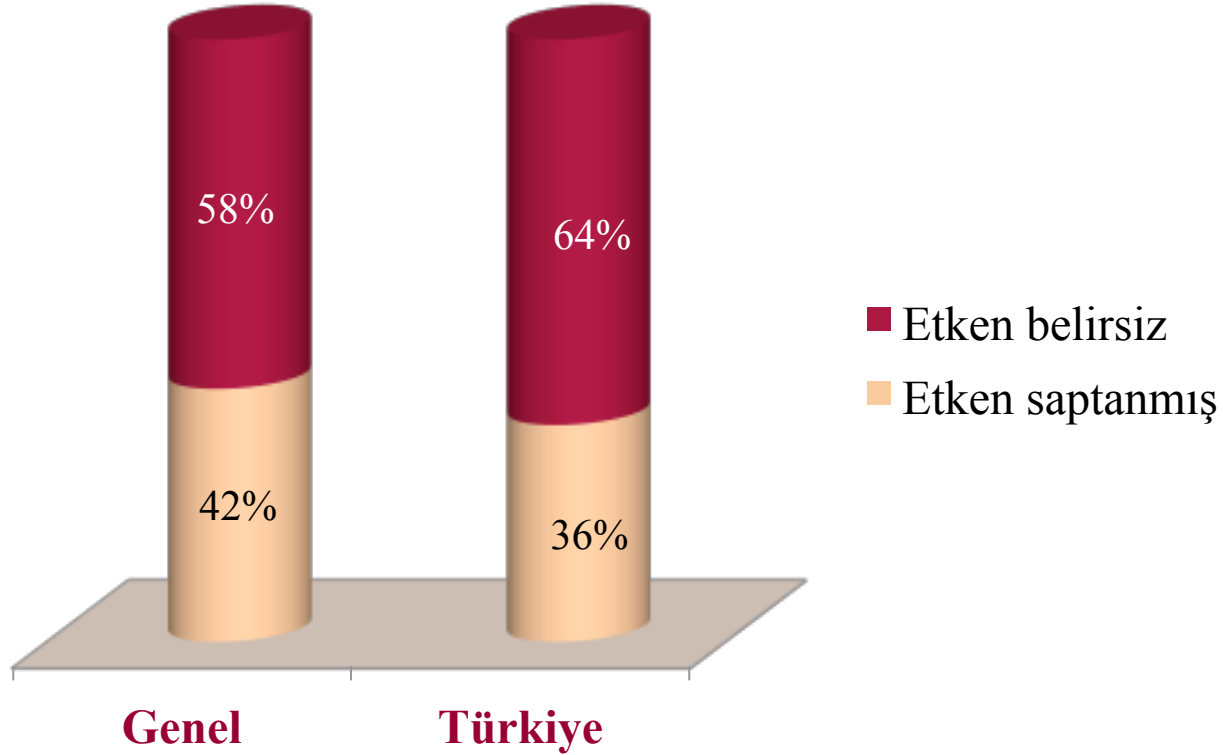
1. Risk analizi
2. Klinik tablo
3. Mikrobiyolojik tanı
4. Radyolojik tanı
5. EEG
6. Sürecin yönetimi, akış şeması

Risk Deęerlendirmesi (ID-IRI)



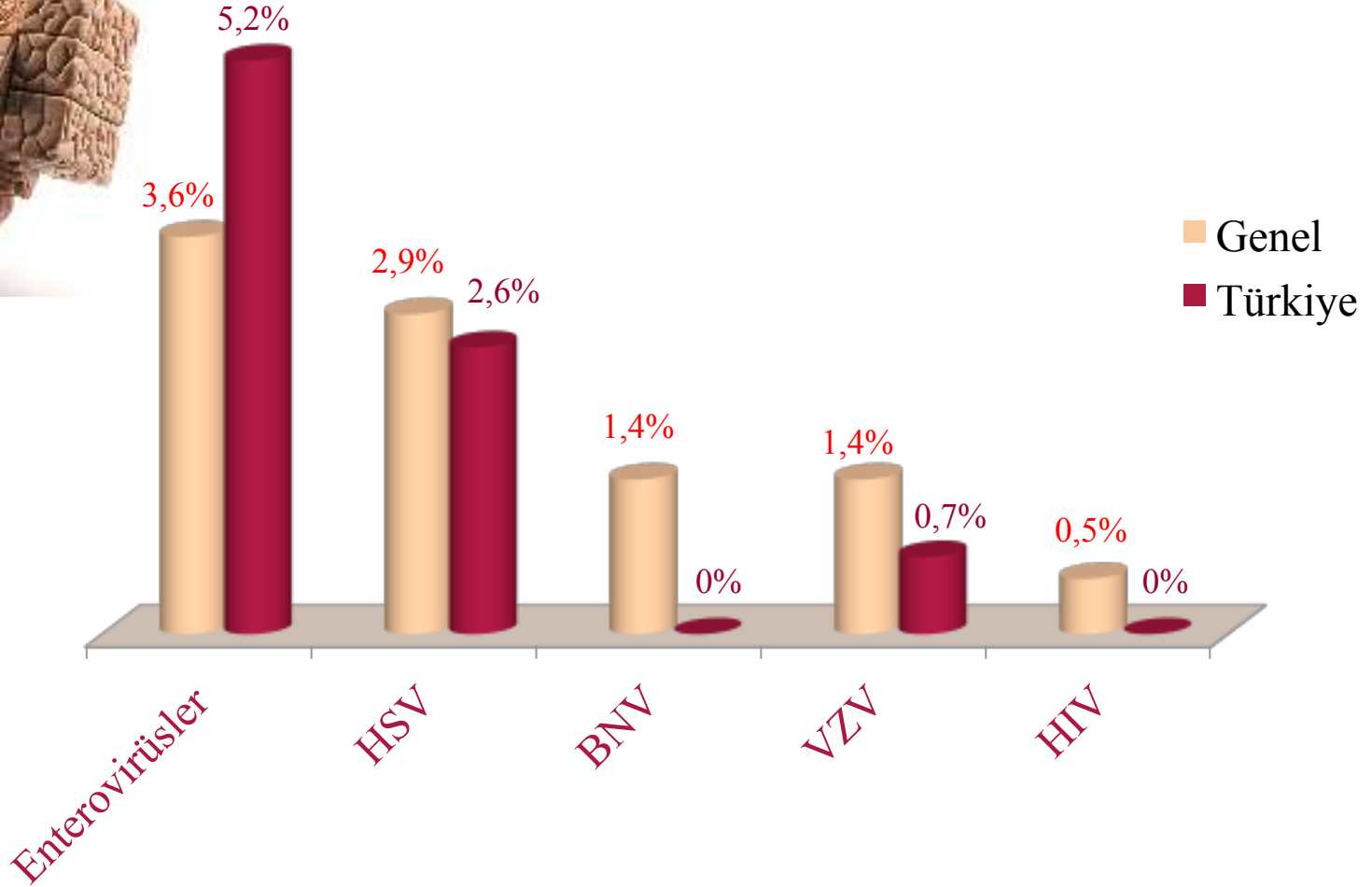
The epidemiology of community acquired central nervous system infections: Data from 20 countries (From Atlantic to Pacific) (yayınlanmamış bilgi)

Mikrobiyolojik Tanı



The epidemiology of community acquired central nervous system infections: Data from 20 countries (From Atlantic to Pacific) (yayınlanmamış bilgi)

Santral Viral Patojenler



The epidemiology of community acquired central nervous system infections: Data from 20 countries (From Atlantic to Pacific) (yayınlanmamış bilgi)

BNV

- Texas % 4, Hırvatistan % 3, Kosova % 8
- Türkiye ?
- Tedavi ?



- Ergunay K, et al. Multicentre evaluation of central nervous system infections due to Flavi and Phleboviruses in Turkey. *J Infect.* 2012;65(4):343-9.
- Erdem H, et al. Emergence and co-infections of WNV and Toscana virus in Eastern Thrace, Turkey. *Clin Microbiol Infect.* 2014;20(4):319-25.
- Ertilav M, et al. Meningoencephalitis caused by WNV in a renal transplant recipient. *Mikrobiyol Bul.* 2014;48(4):674-82.

Akılcı Antiviral Kullanımı



HSV, nasıl bir ensefalit?

Antiviral Öncesi

- %70 ölüm



Asiklovir ile

- % 5 ölüm, % 90 sekel¹
- % 10 ölüm, % 75 sekel²
- % 15 ölüm, % 20 sekel³

Stahl JP, et al. 2012. Herpes simplex encephalitis and management of acyclovir in encephalitis patients in France. Epidemiol Infect 140:372–381.

Dagsdóttir HM, et al. 2014. Herpes simplex encephalitis in Iceland 1987–2011. Springerplus 3:524.

Raschilas F, et al. Outcome of and prognostic factors for herpes simplex encephalitis in adult patients: results of a multicenter study. Clin Infect Dis. 2002 Aug 1;35(3):254-60.

Herpetik Meningoensefalitler



501, PCR (+) vaka



Results of a Multinational Study Suggest the Need for Rapid Diagnosis and Early Antiviral Treatment at the Onset of Herpetic Meningoencephalitis

Hakan Erdem,^a Yasemin Cag,^b Derya Ozturk-Engin,^c Sylviane Defres,^{d,e} Selcuk Kaya,^f Lykke Larsen,^g Mario Poljak,^h Bruno Barsic,ⁱ Xavier Argemi,^j Signe Maj Sørensen,^k Anne Lisbeth Bohr,^l Pierre Tattevin,^m Jesper Damsgaard Gunst,ⁿ Lenka Baštáková,^o Matjaž Jereb,^p Isik Somuncu Johansen,^q Oguz Karabay,^q Abdullah Umut Pekok,^r Oguz Resat Sipahi,^s Mahtab Chehri,^t Guillaume Beraud,^u Ghaydaa Shehata,^v Rosa Fontana Del Vecchio,^w Mauro Maresca,^w Hasan Karsen,^x Gonul Sengoz,^y Mustafa Sunbul,^z Gulden Yilmaz,^{aa} Hava Yilmaz,^z Ahmad Sharif-Yakan,^{bb} Souha Shararah Kanj,^{bb} Emine Parlak,^{cc} Filiz Pehlivanoglu,^y Fatime Korkmaz,^{dd} Suheyla Komur,^{ee} Sukran Kose,^{ff} Mehmet Ulug,^{gg} Sibel Bolukcu,^{cc} Seher Ayten Coskuner,^{hh} Nevin Ince,ⁱⁱ Yasemin Akkoyunlu,^{jj} Gulistan Halac,^{kk} Elif Sahin-Horasan,^{ll} Hulya Tireli,^{mm} Gamze Kilicoglu,ⁿⁿ Akram Al-Mahdawi,^{oo} Salih Atakan Nemli,^{pp} Asuman Inan,^c Seniha Senbayrak,^c Jean Paul Stahl,^{qq} Haluk Vahaboglu^{rr}

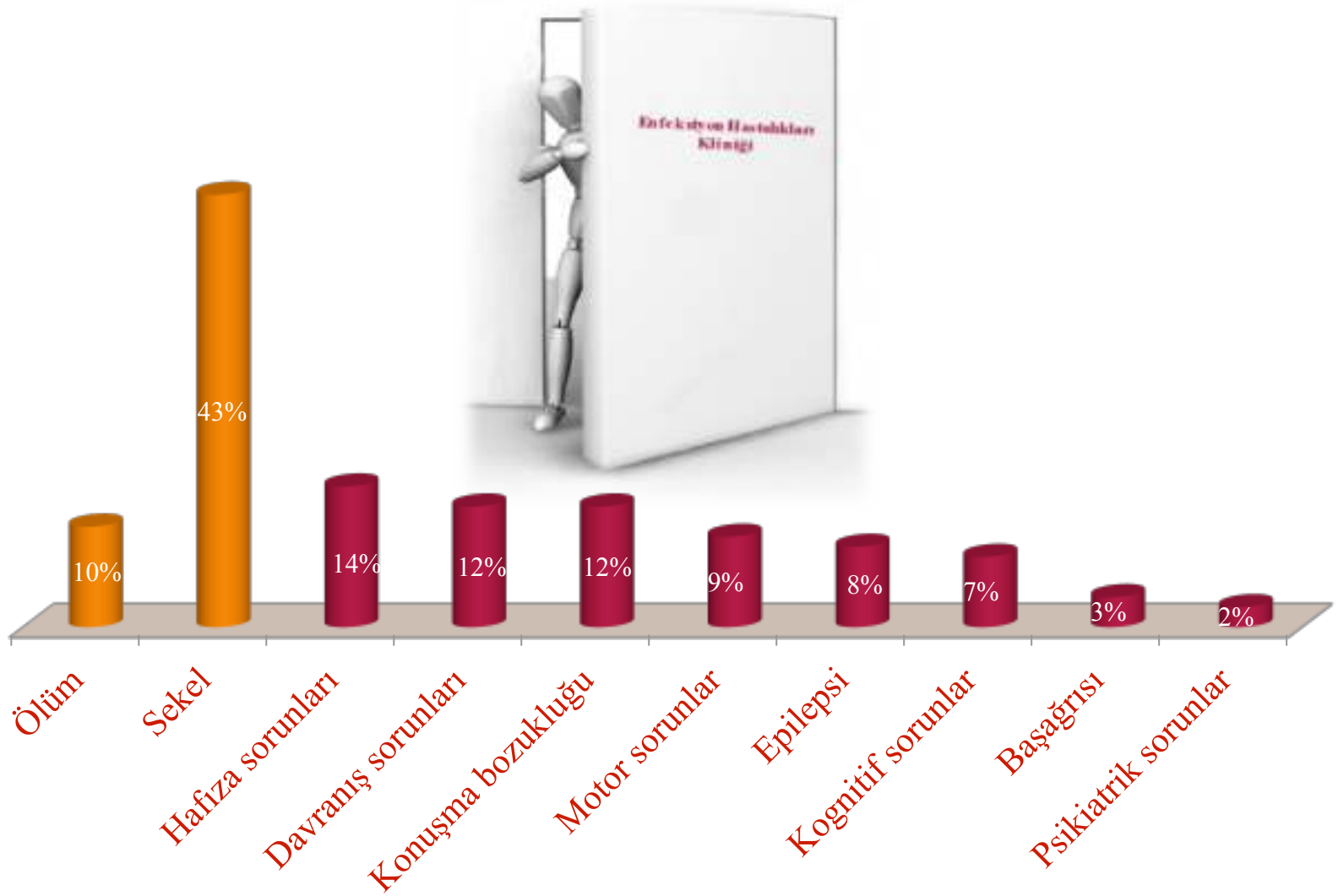
Accepted Manuscript ID-IRI ve ESGIB ortak çalışması, 496 vaka

Managing Atypical and Typical herpetic central nervous system infections: results of A Multinational study

Yasemin Cag, Hakan Erdem, Stephen Leib, Sylviane Defres, Selcuk Kaya, Lykke Larsen, Mario Poljak, Derya Ozturk-Engin, Bruno Barsic, Xavier Argemi, Signe Maj Sørensen, Anne Lisbeth Bohr, Pierre Tattevin, Jesper Damsgaard Gunst, Lenka Baštáková, Matjaž Jereb, Isik Somuncu Johansen, Oguz Karabay, Abdullah Umut Pekok, Oguz Resat Sipahi, Mahtab Chehri, Guillaume Beraud, Ghaydaa Shehata, Rosa Fontana, Mauro Maresca, Hasan Karsen, Gonul Sengoz, Mustafa Sunbul, Gulden Yilmaz, Hava Yilmaz, Ahmad Sharif-Yakan, Souha Kanj, Emine Parlak, Filiz Pehlivanoglu, Fatime Korkmaz, Suheyla Komur, Sukran Kose, Mehmet Ulug, Sibel Bolukcu, Seher Ayten Coskuner, Jean Paul Stahl, Nevin Ince, Yasemin Akkoyunlu, Gulistan Halac, Elif Sahin-Horasan, Hulya Tireli, Gamze Kilicoglu, Akram Al-Mahdawi, Salih Atakan Nemli, Asuman Inan, Seniha Senbayrak, Haluk Vahaboglu, Nazif Elaldi



Taburcu Olurken...



Erdem H, Cag Y, Ozturk-Engin, et al. Results of a multinational study suggest rapid diagnosis and early onset of antiviral treatment in herpetic meningoencephalitis. Antimicrobial Agents and Chemotherapy 2015;59(6):3084-9.

HSV Ensefaliti, Seyir

TABLE 3 Final model, including independent predictors of unfavorable outcome

Variable	OR ^a	95% CI		P
		Low	High	
Age (yr)	1.04	1.02	1.05	0.000
Glasgow Coma Scale score	0.84	0.77	0.93	0.000
Elapsed time (days) ^b				
>2 and ≤7	1.80	1.16	2.79	0.009
>7	3.75	1.72	8.15	0.001

^a OR, odds ratio.

^b Elapsed time between onset of symptoms and administration of antiviral treatment.

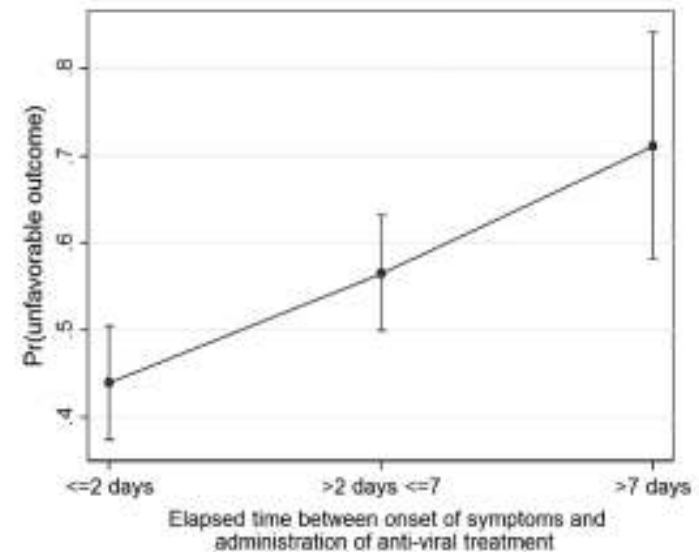


FIG 1 Predictions (Pr, probability) of antiviral treatment timing for unfavorable outcome. The data are presented as the mean values with the 95% CI.

Erdem H, Cag Y, Ozturk-Engin, et al. Results of a multinational study suggest rapid diagnosis and early onset of antiviral treatment in herpetic meningoencephalitis. Antimicrobial Agents and Chemotherapy 2015;59(6):3084-9.

Kime antiviral verelim?



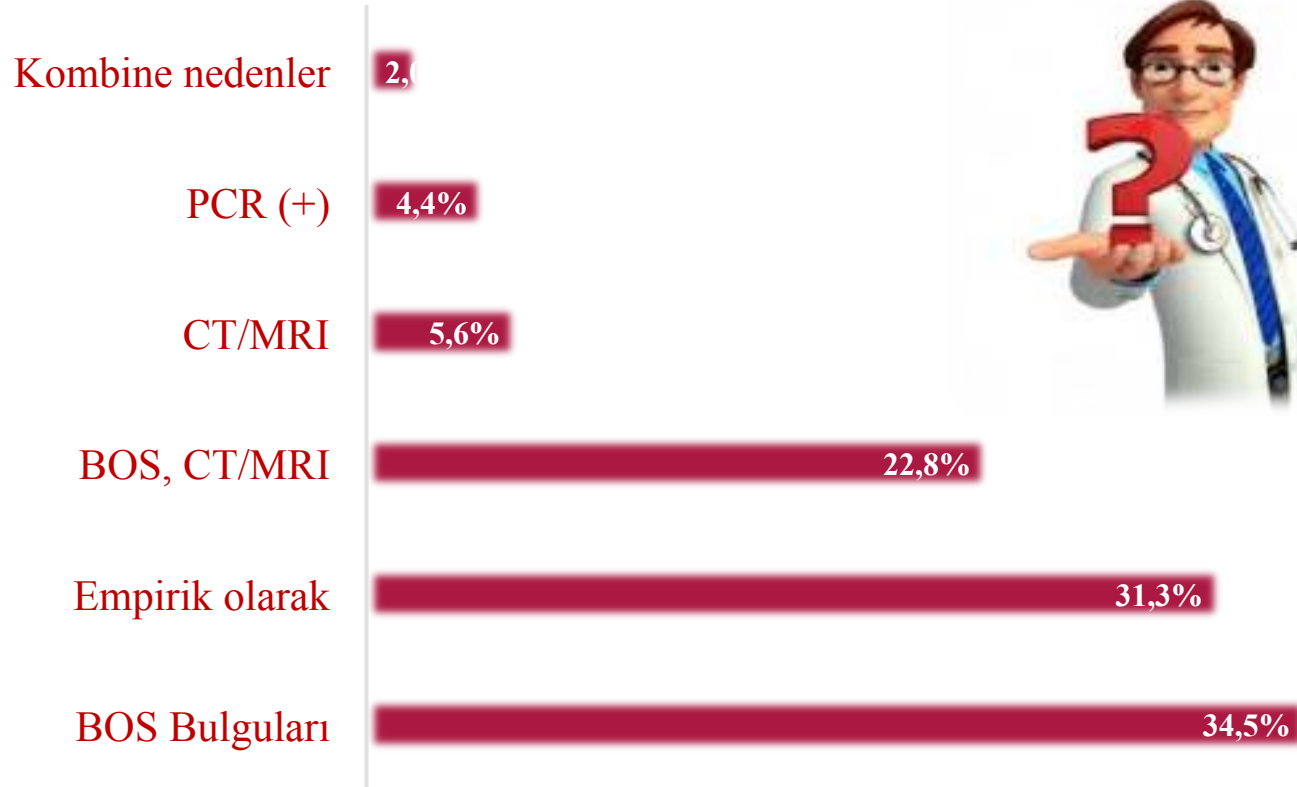
Despite the wide range of viruses that have been reported to cause encephalitis, specific antiviral therapy is generally limited to infections caused by the herpesviruses—specifically, herpes simplex virus—and HIV. Acyclovir treatment should be initiated in all patients with suspected encephalitis, pending results of diagnostic studies. During the appropriate season, patients who present with clinical clues suggestive of rickettsial or ehrlichial infection should be treated empirically with doxycycline. Empirical therapy for acute bacterial meningitis should also be initiated if clinically indicated. In patients with acute disseminated encephalomyelitis, corticosteroids are recommended; plasma exchange should be considered in patients who do not respond to this treatment.

Tunkel AR, et al. Infectious Diseases Society of America. The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2008 Aug 1;47(3):303-27.

Şüpheli ensefalit nedir?



Antiviral Başlama Gerekçeleri

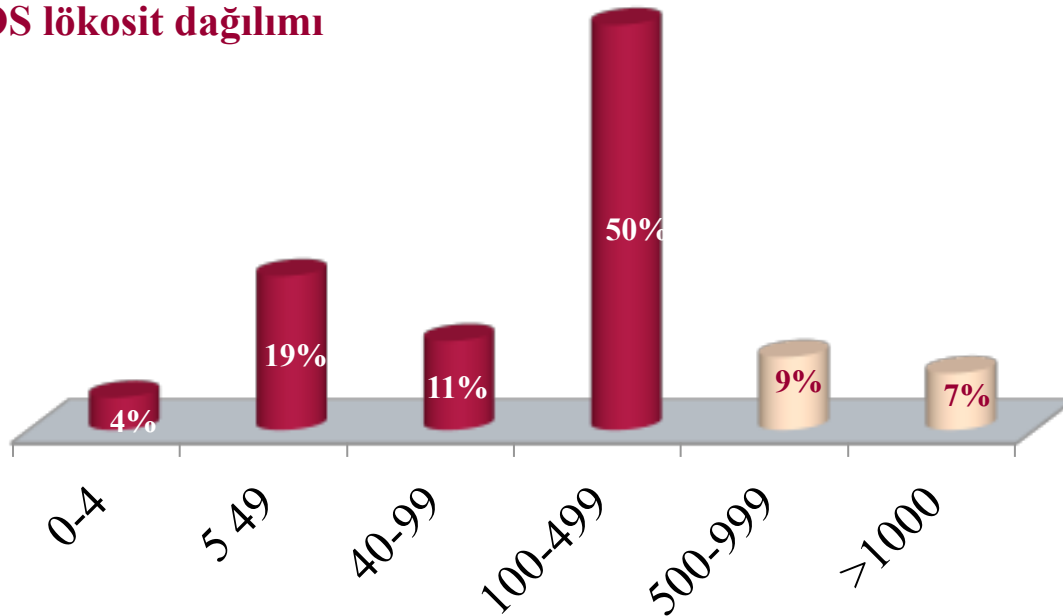


ID-IRI HSV Ensefaliti veri tabanı

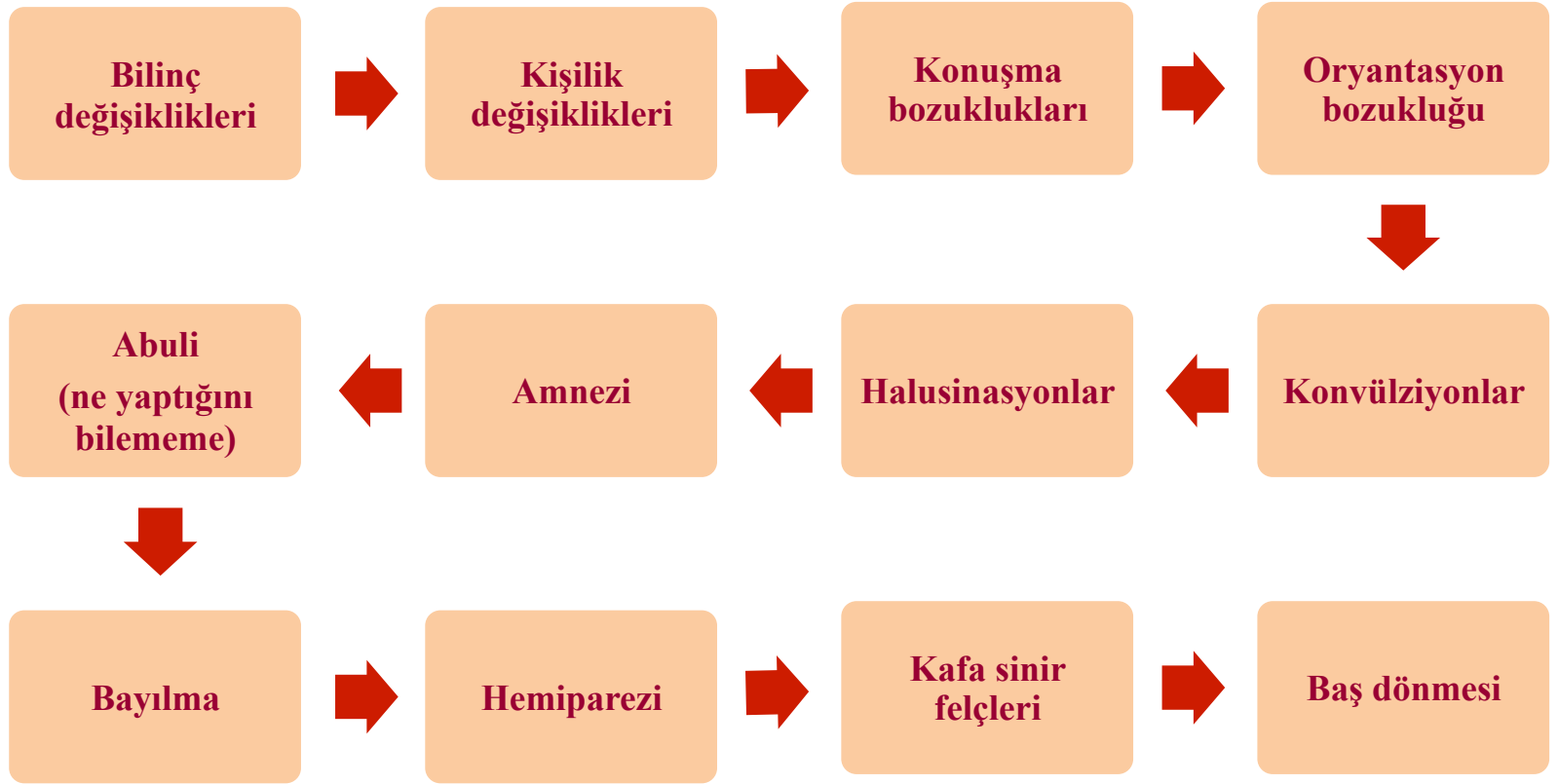
Medyan (IQR)

Kan lökosit sayımı ($\times 10^3 / \text{mm}^3$)	9.7 (7.5–13.0)
CRP (mg / L)	0.8 (0.2–2.0)
ESR (mm/h)	19.0 (11.8–30.0)
BOS/Serum glu oranı < 0.60	50.2%
BOS proteini (> 45 mg/dL)	77.6%

BOS lökosit dağılımı



Ensefalit (beyin parankimi tutulumu) bulguları nelerdir?



Ensefalit Yakınma ve Bulguları

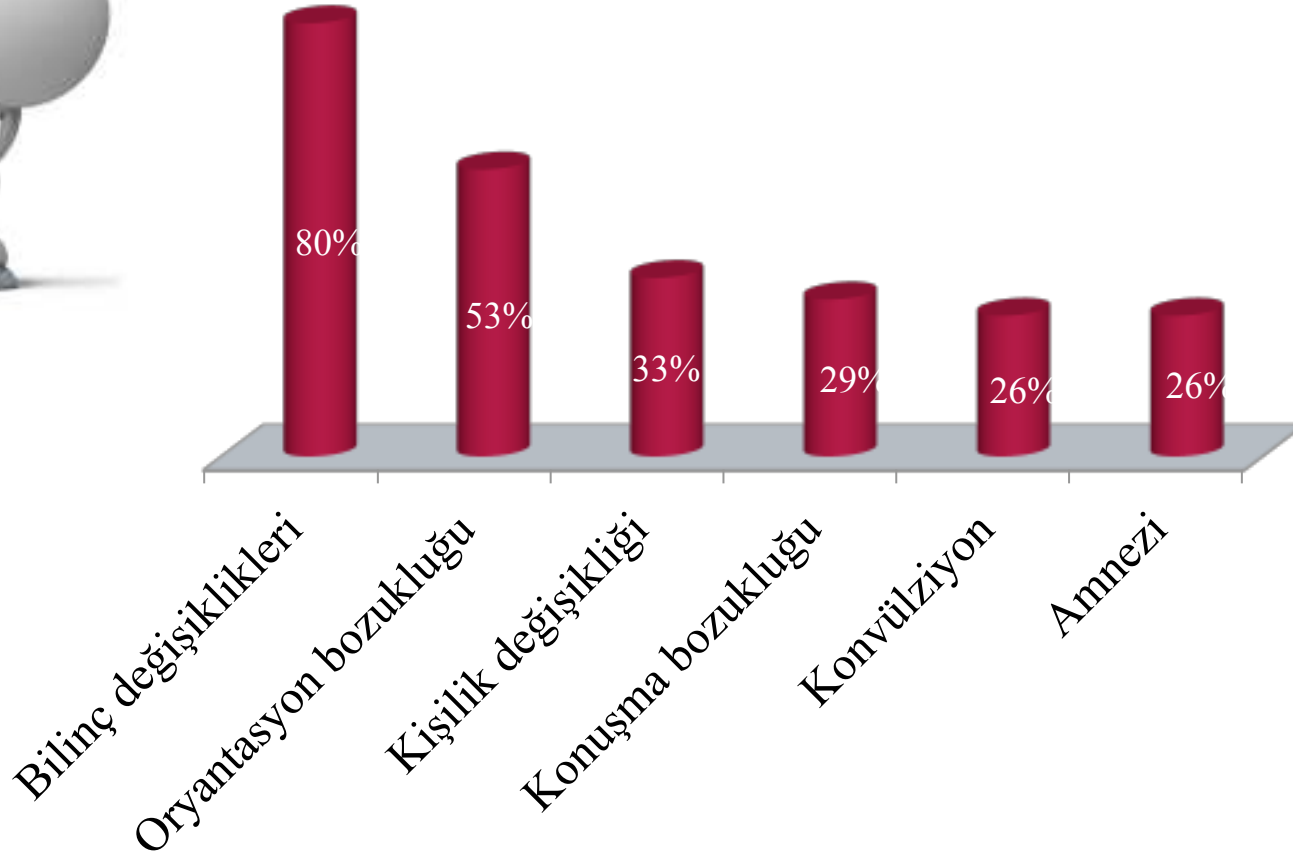


- Mevcut
- Mevcut deęil

Her SSS enfeksiyonu şüphesinde antiviral verilmeli mi?

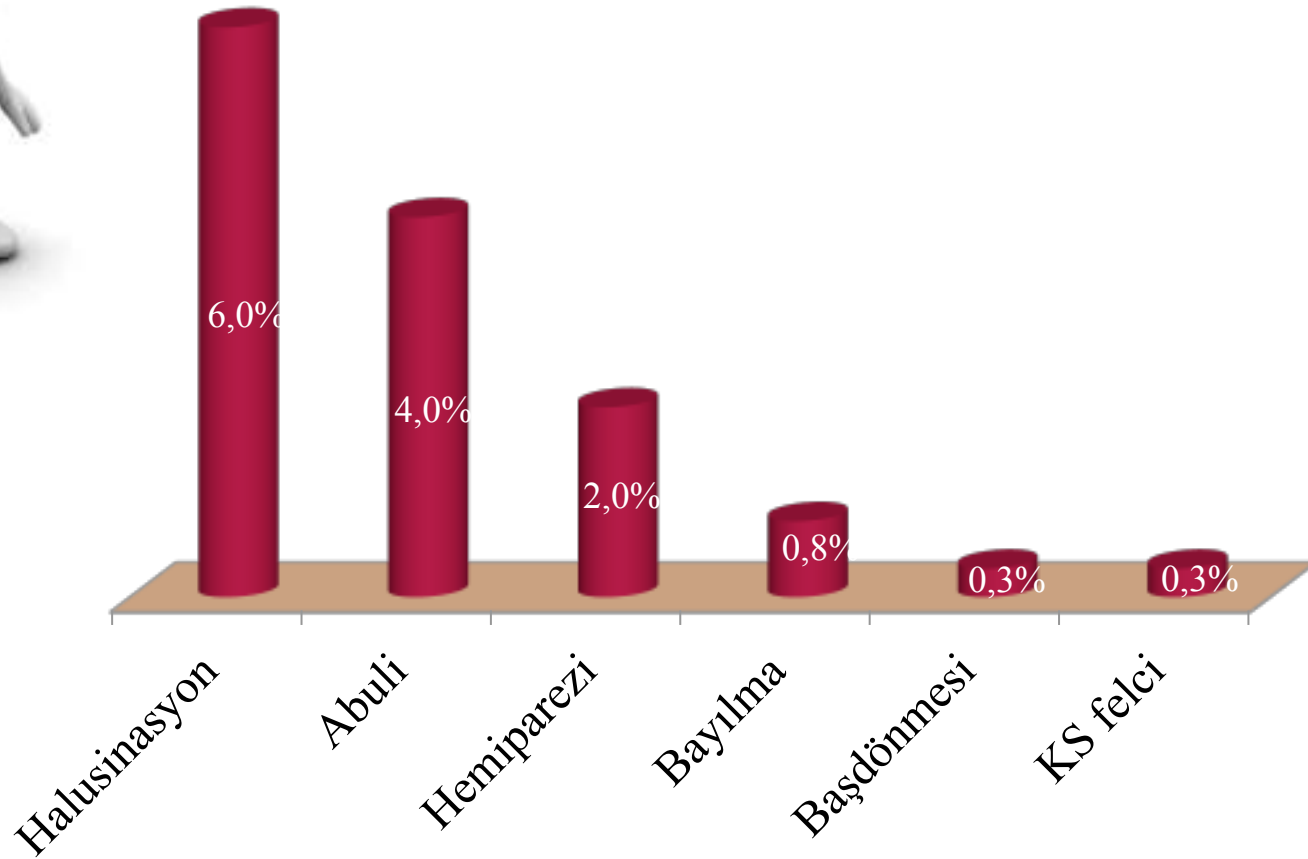


Ensefalitle Uyumlu Vakalar Sık Bulgular



Erdem H, Cag Y, Ozturk-Engin, et al. Results of a multinational study suggest rapid diagnosis and early onset of antiviral treatment in herpetic meningoencephalitis. Antimicrobial Agents and Chemotherapy 2015;59(6):3084-9.

Ensefalit, Nadir Bulgular

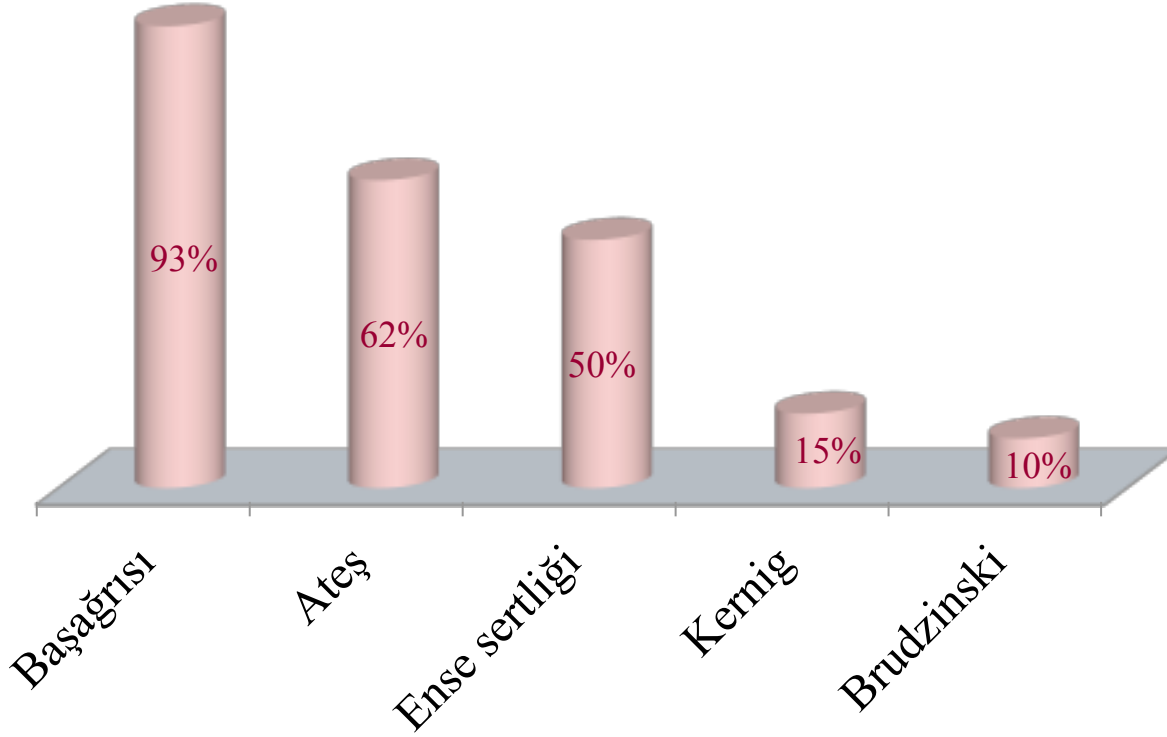


Bilinç Deęişiklikleri

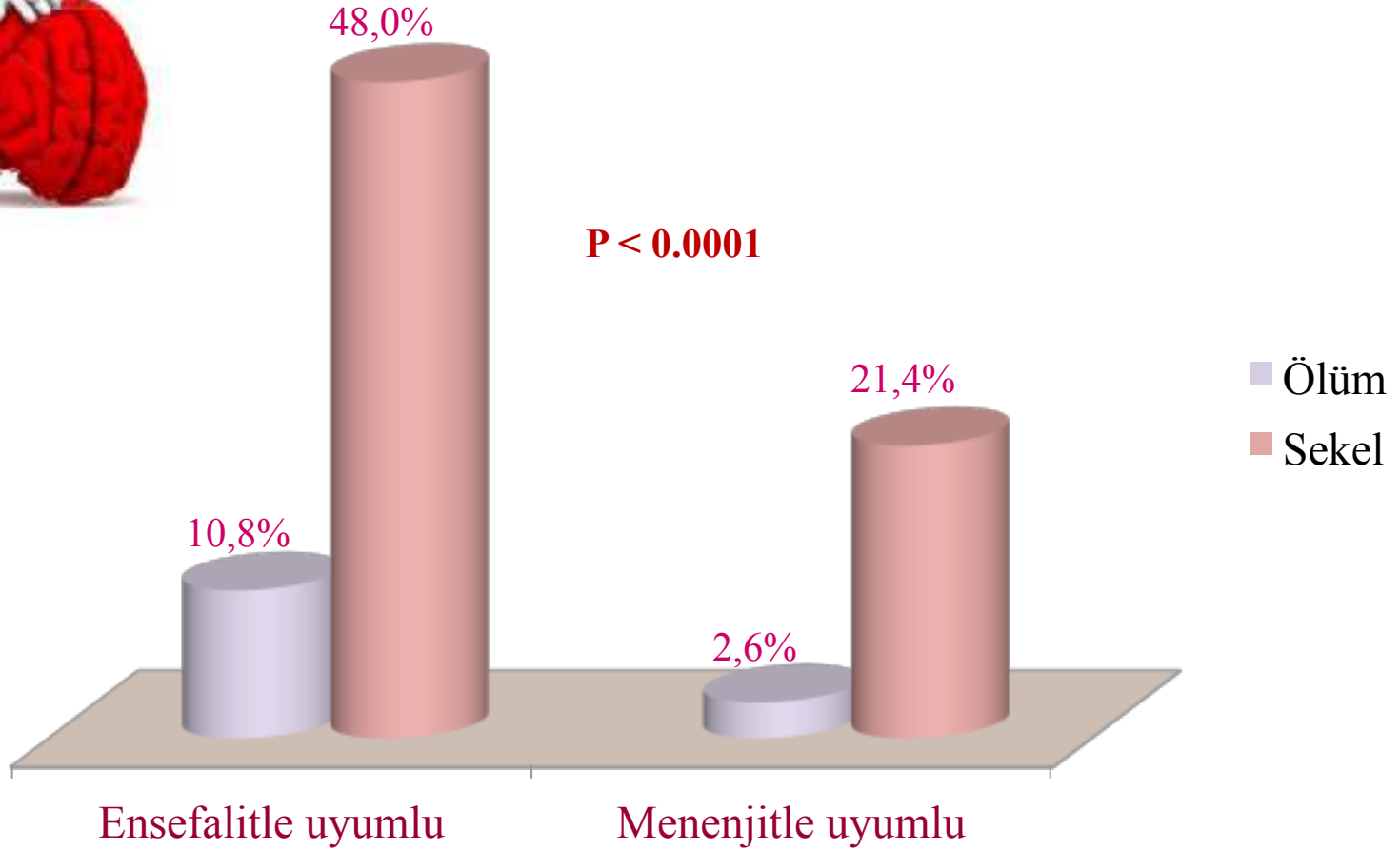


Glasgow Koma Ölçümü Ortanca [IQR]: 14 (13-15)

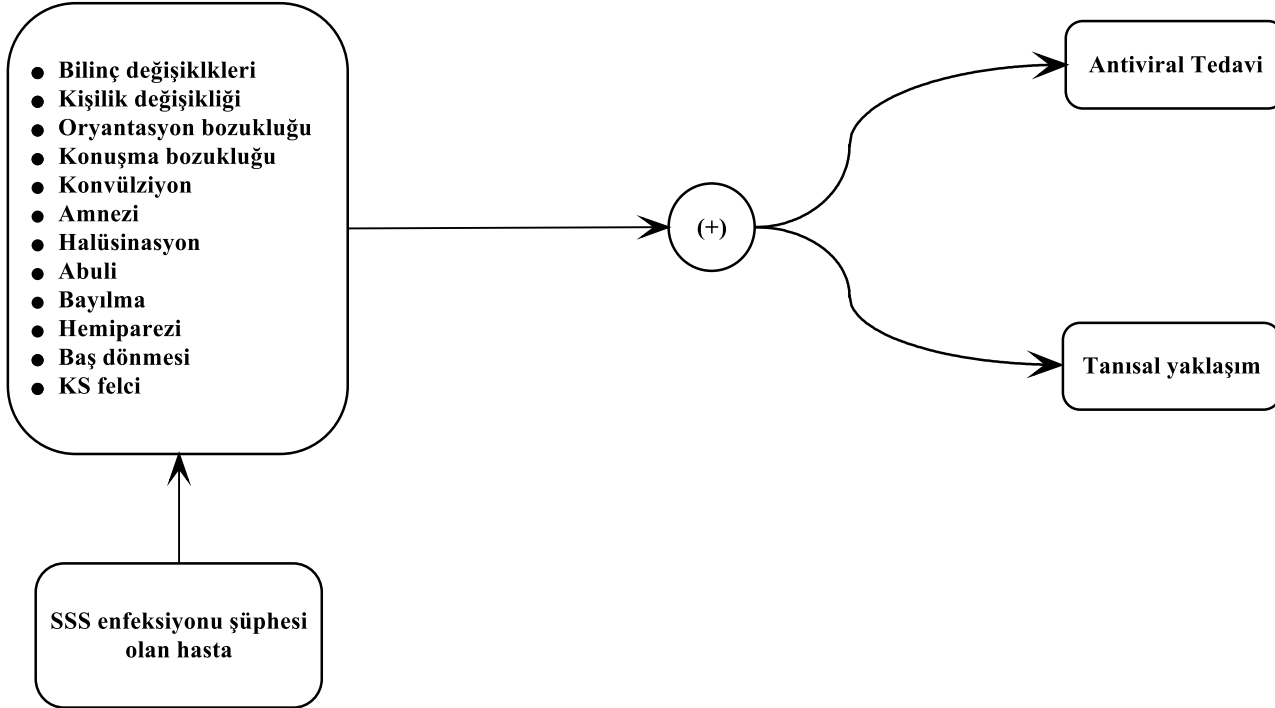
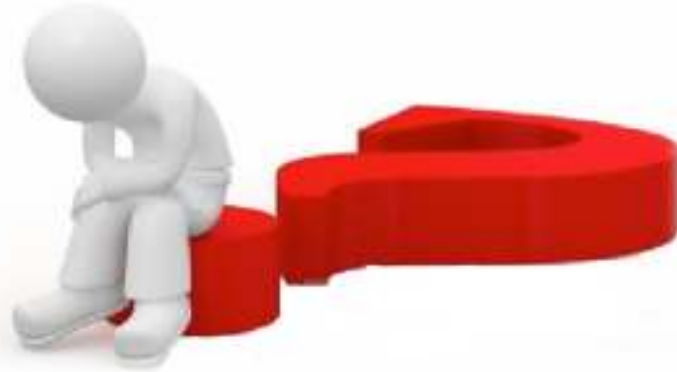
Ensefalit Bulgusu Olmayanlar

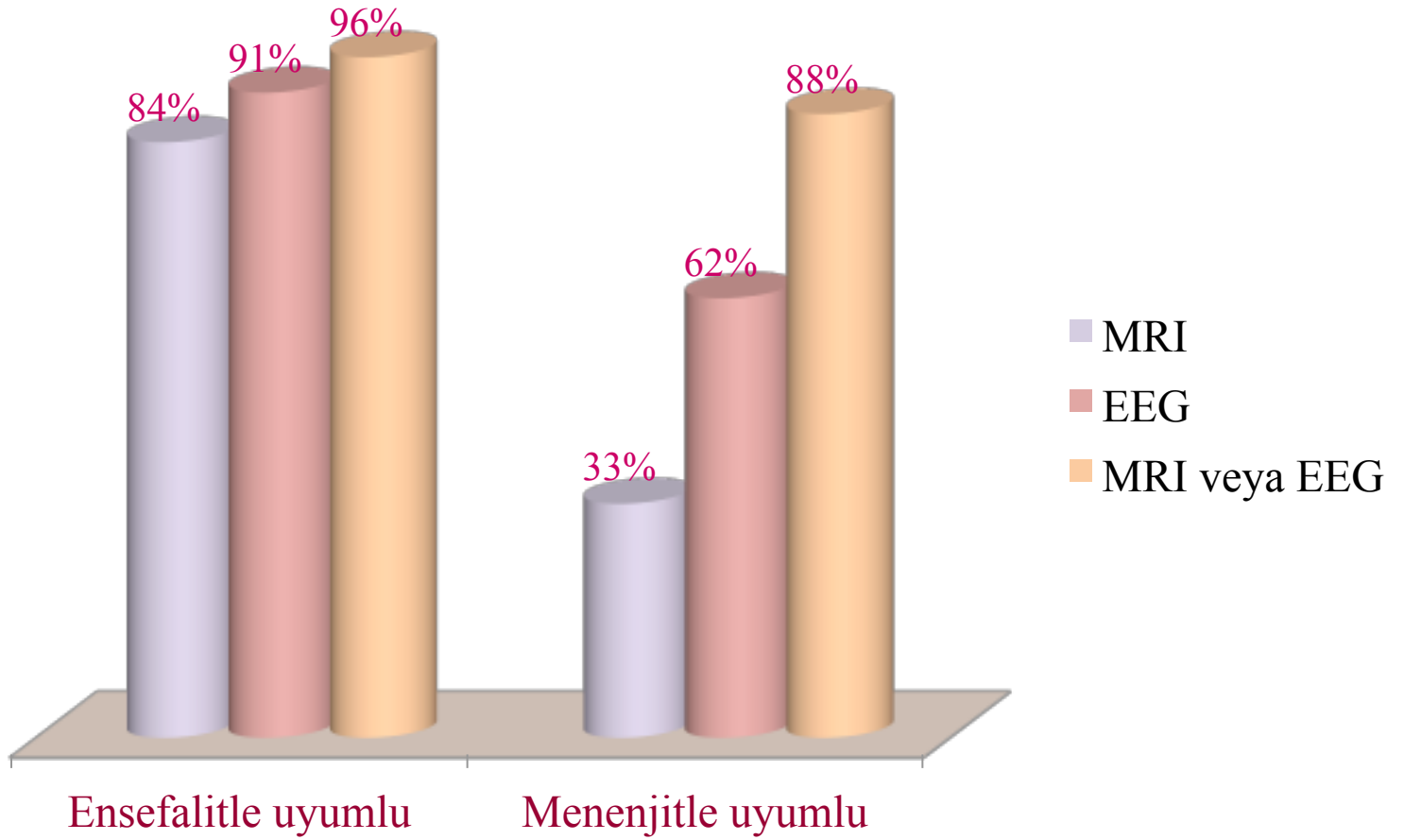


Menenjit?

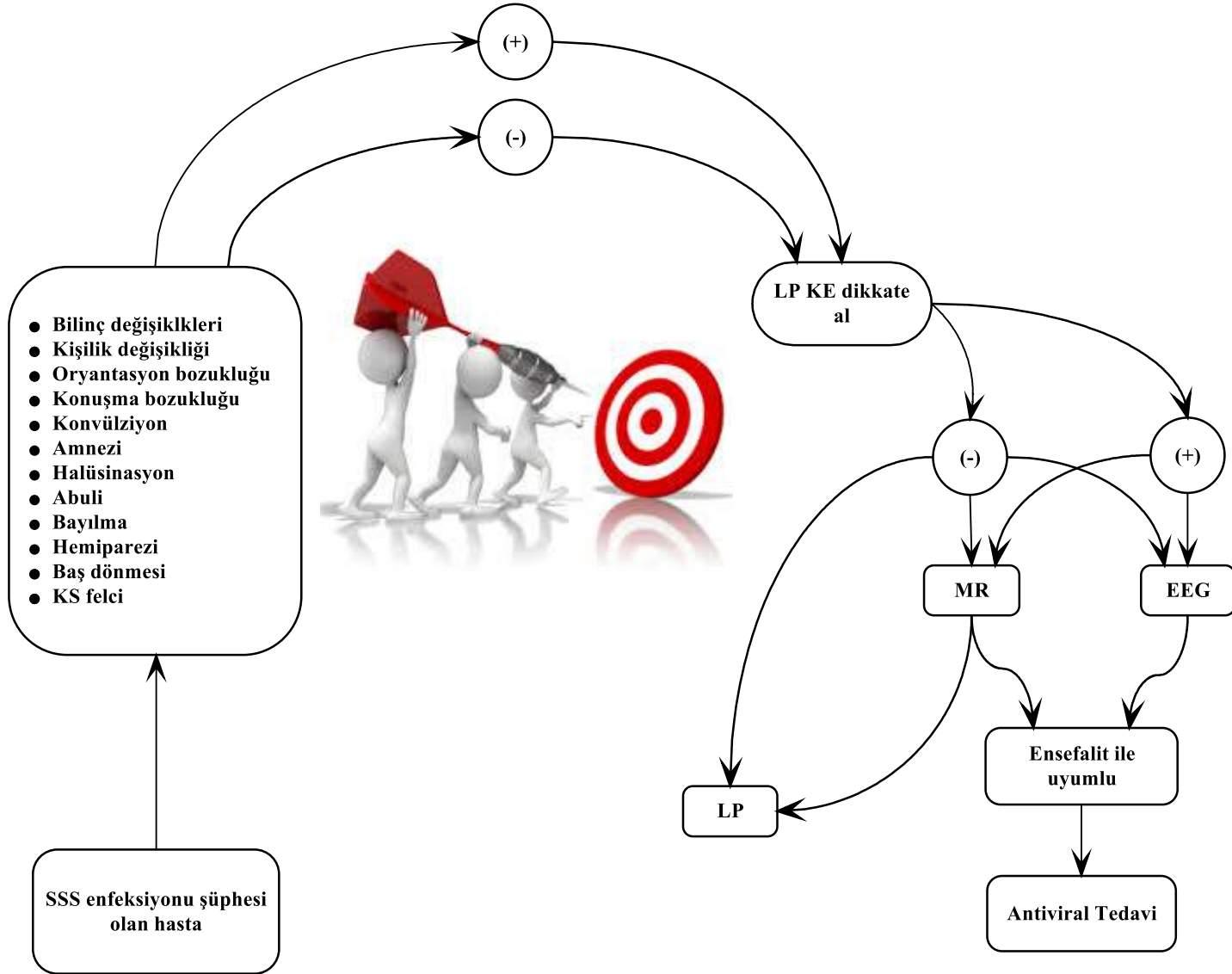


Çağ Y, Erdem H, Leib S, et al. Managing atypical and typical Herpetic central nervous system infections: Results of a multinational study. Clinical Microbiology and Infection (Yayında).

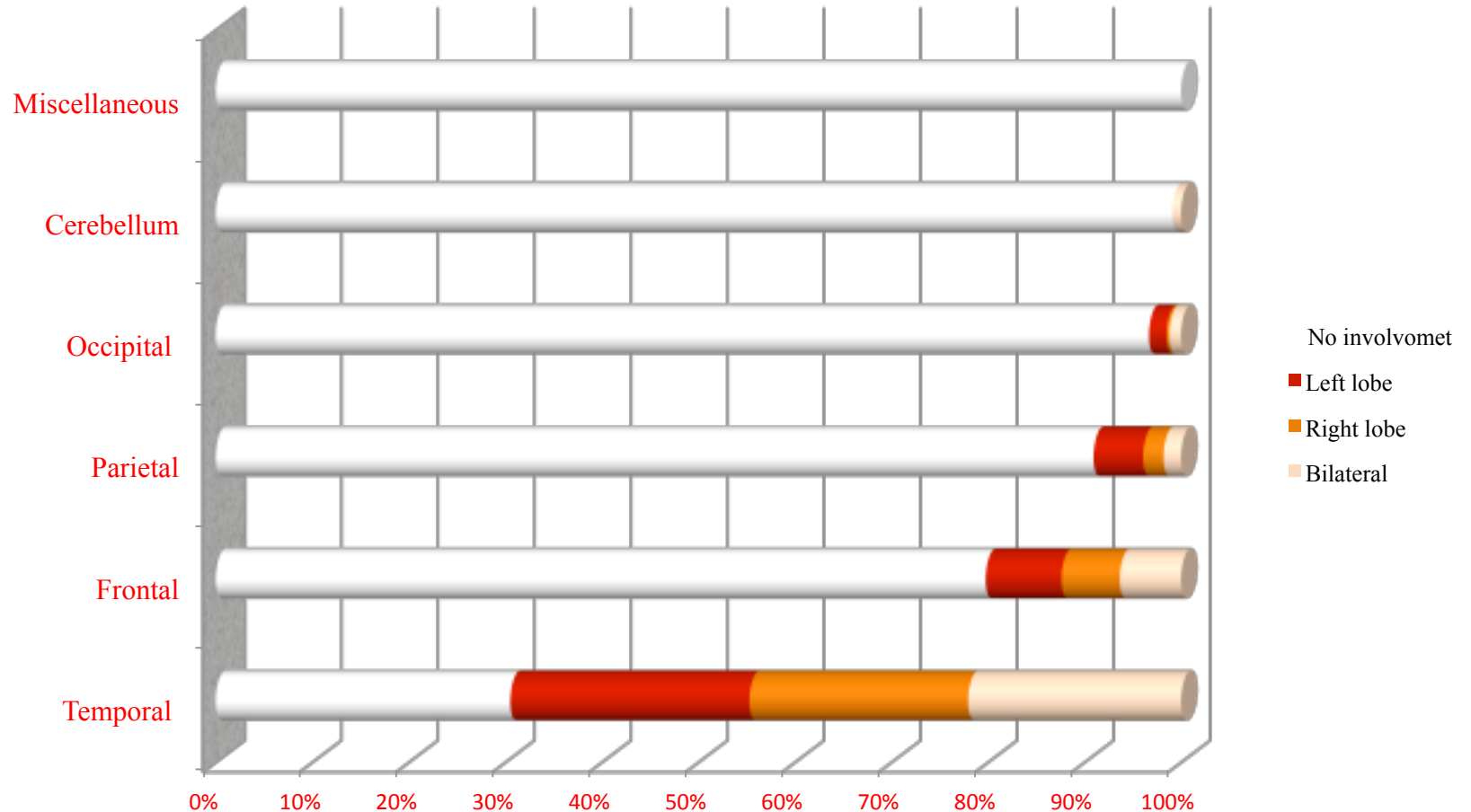




Çağ Y, Erdem H, Leib S, et al. Managing atypical and typical Herpetic central nervous system infections: Results of a multinational study. Clinical Microbiology and Infection (Yayında).

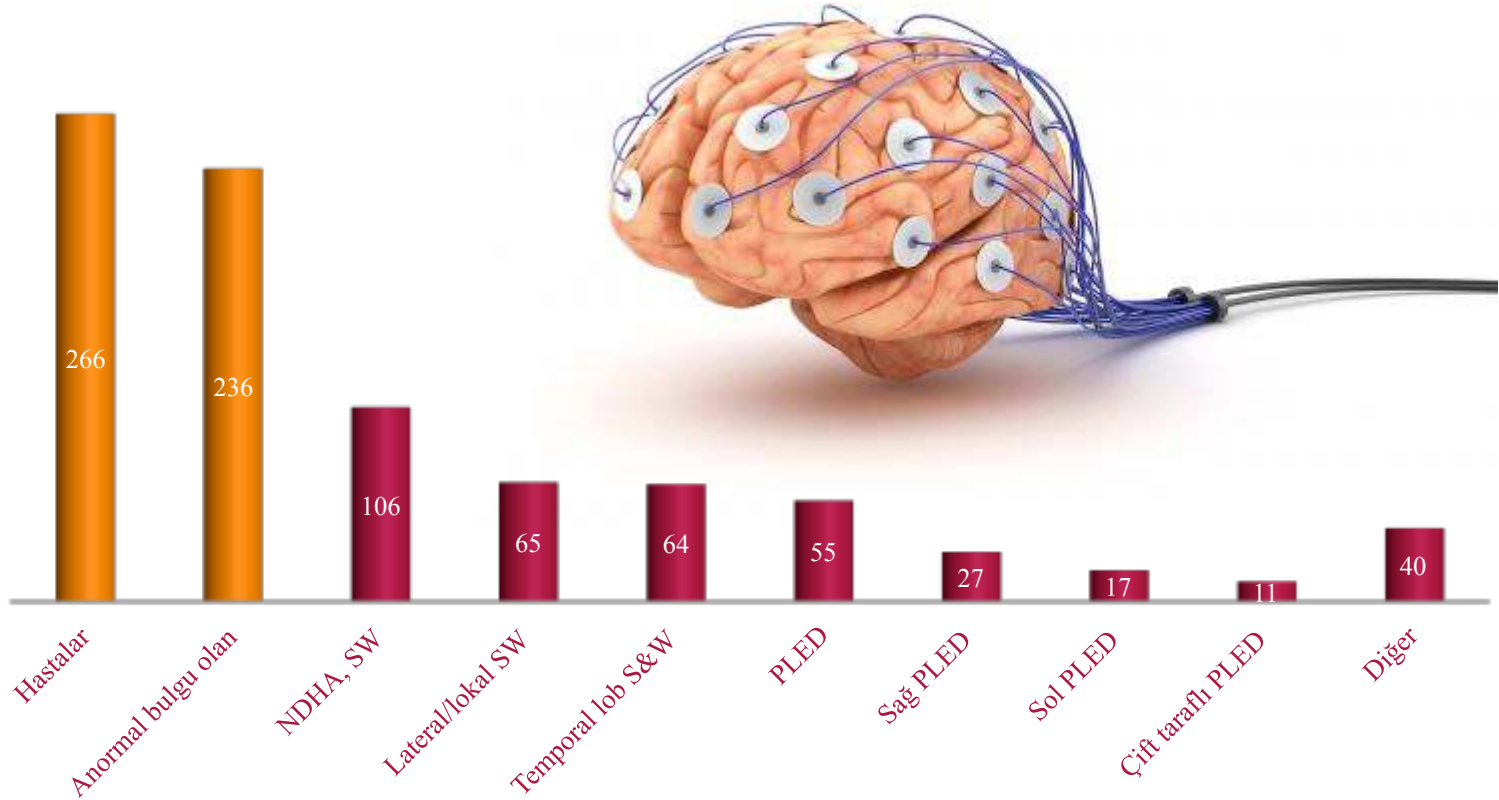


MR Bulguları



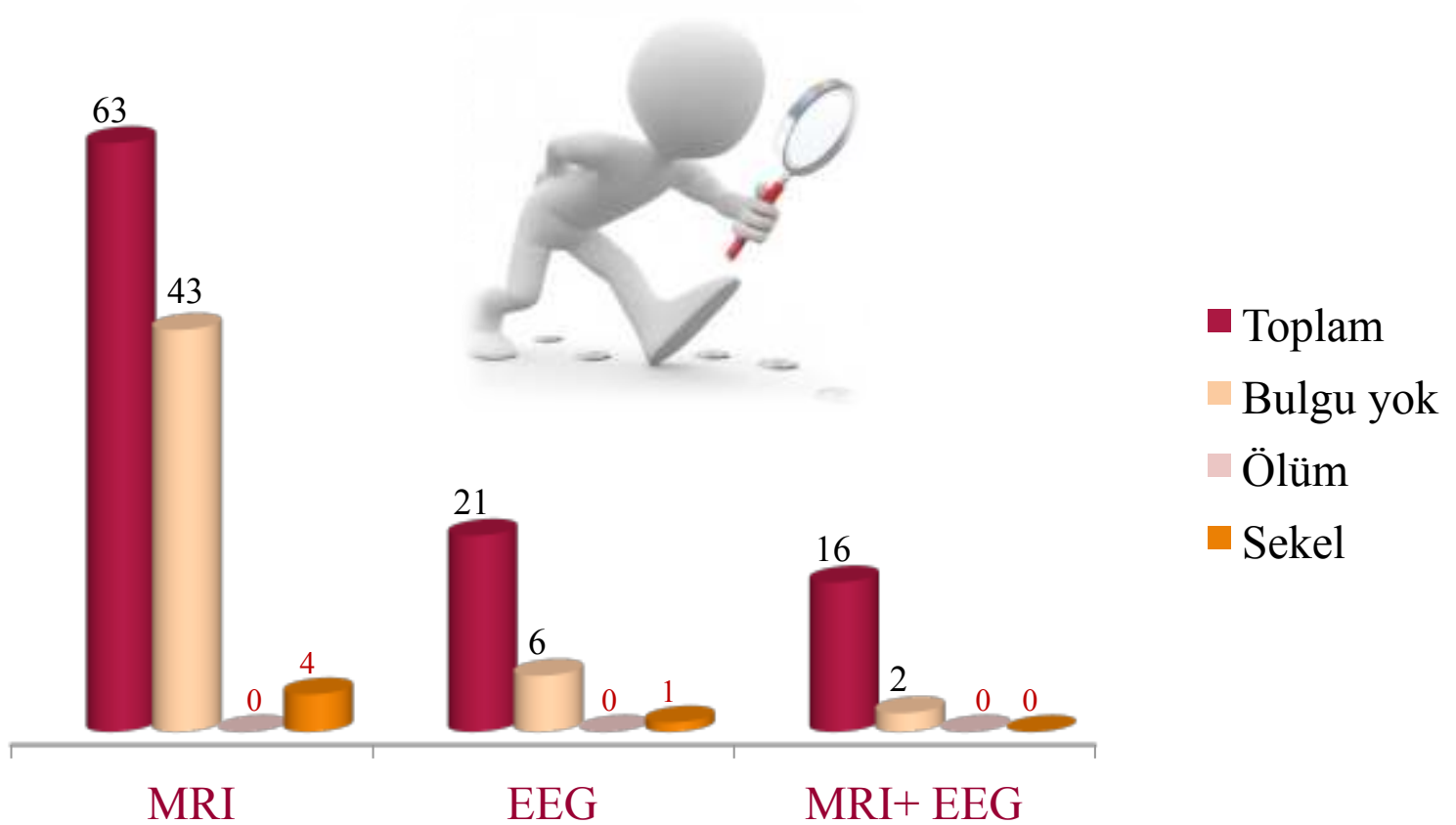
Çag Y, Erdem H, Leib S, et al. Managing atypical and typical Herpetic central nervous system infections: Results of a multinational study. Clinical Microbiology and Infection (Yayında).

EEG Bulguları

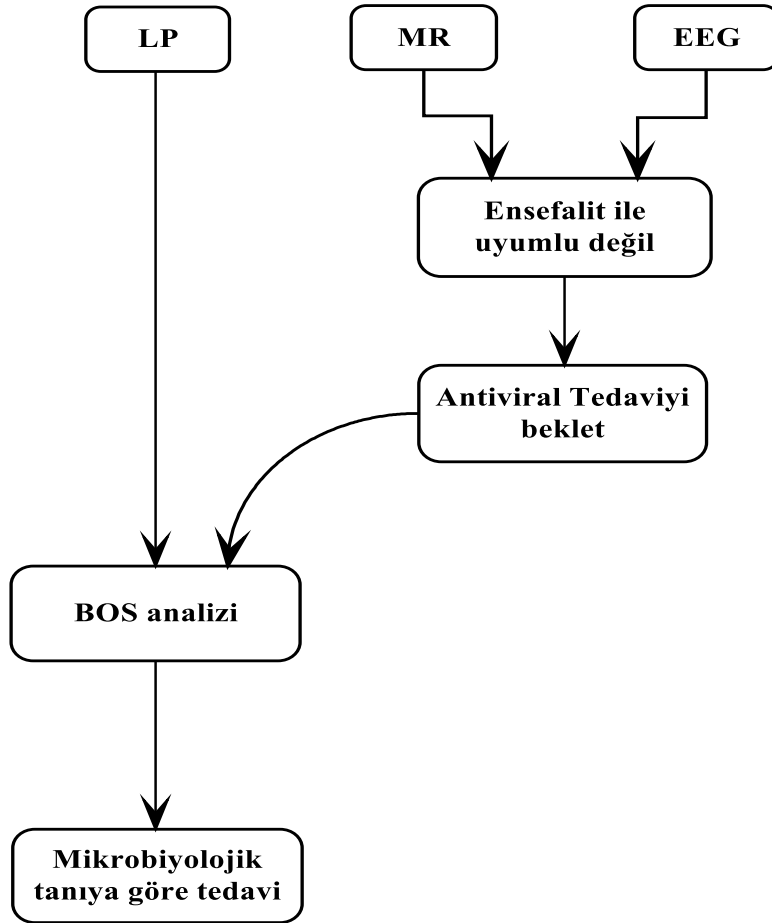


Çağ Y, Erdem H, Leib S, et al. Managing atypical and typical Herpetic central nervous system infections: Results of a multinational study. Clinical Microbiology and Infection (Yayında).

Menenjitle Uyumlu Vakalar (EEG, MR uyumsuz)

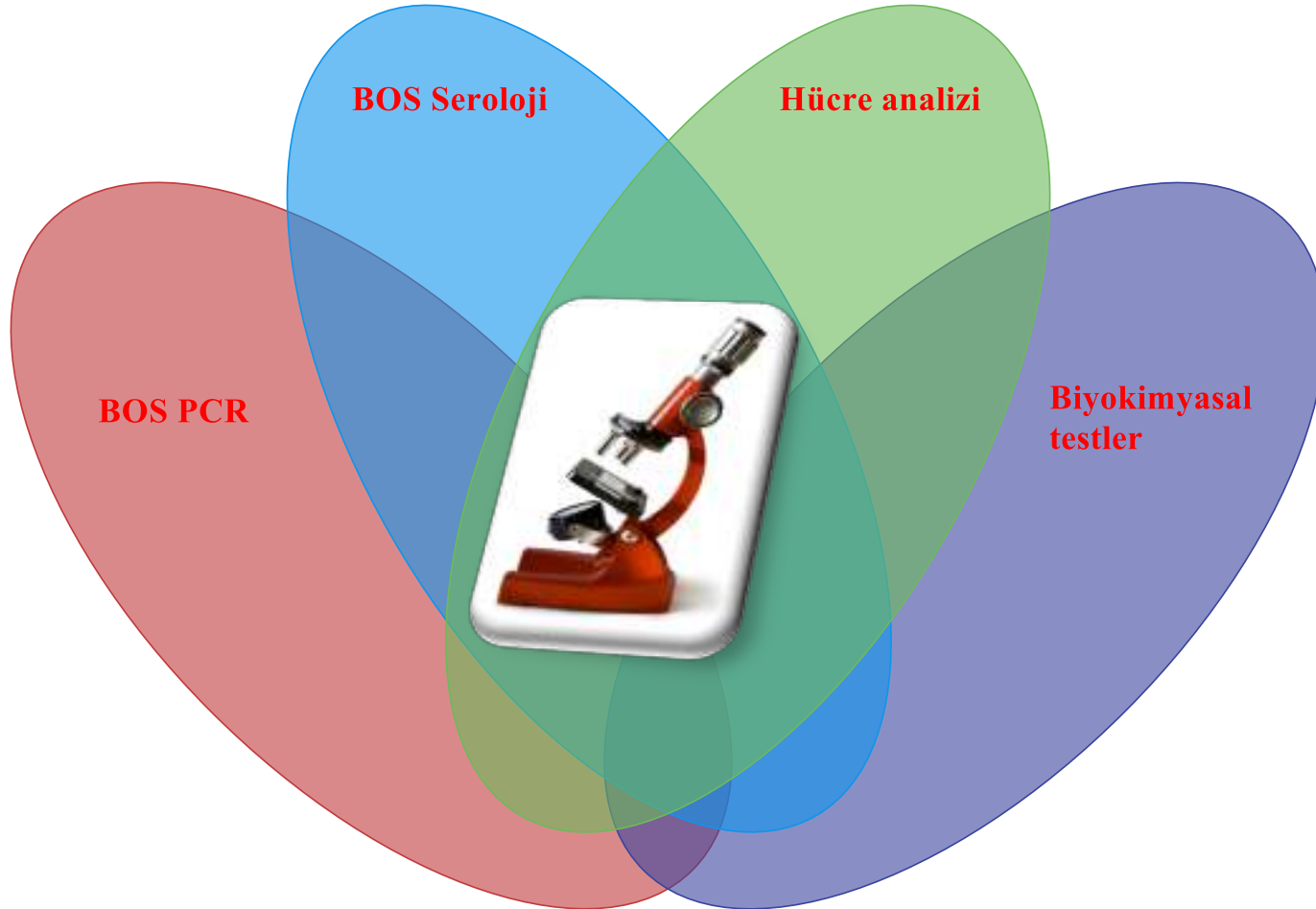


Menenjitle Uyumlu Vakalar



Her SSS enfeksiyonunda empirik asiklovir...

Laboratuvar Tanı



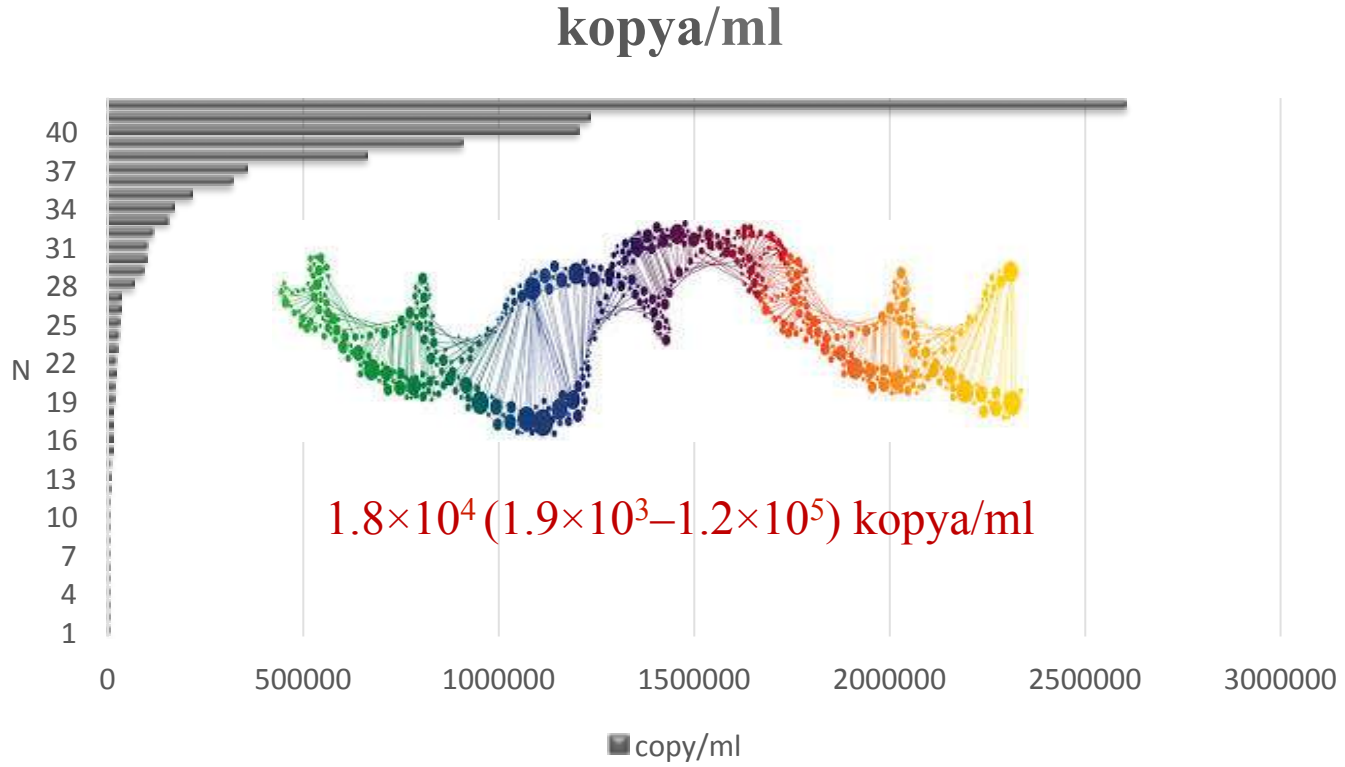
HSV PCR



- Sensitivite % 95-100
- Spesifite % 94-100

Stahl JP, et al. HSV encephalitis and management of acyclovir in encephalitis patients in France. Epidemiol Infect. 2012 ;140(2):372-81.

HSV Viral Yük



ID-IRI HSV Ensefaliti veri tabanı

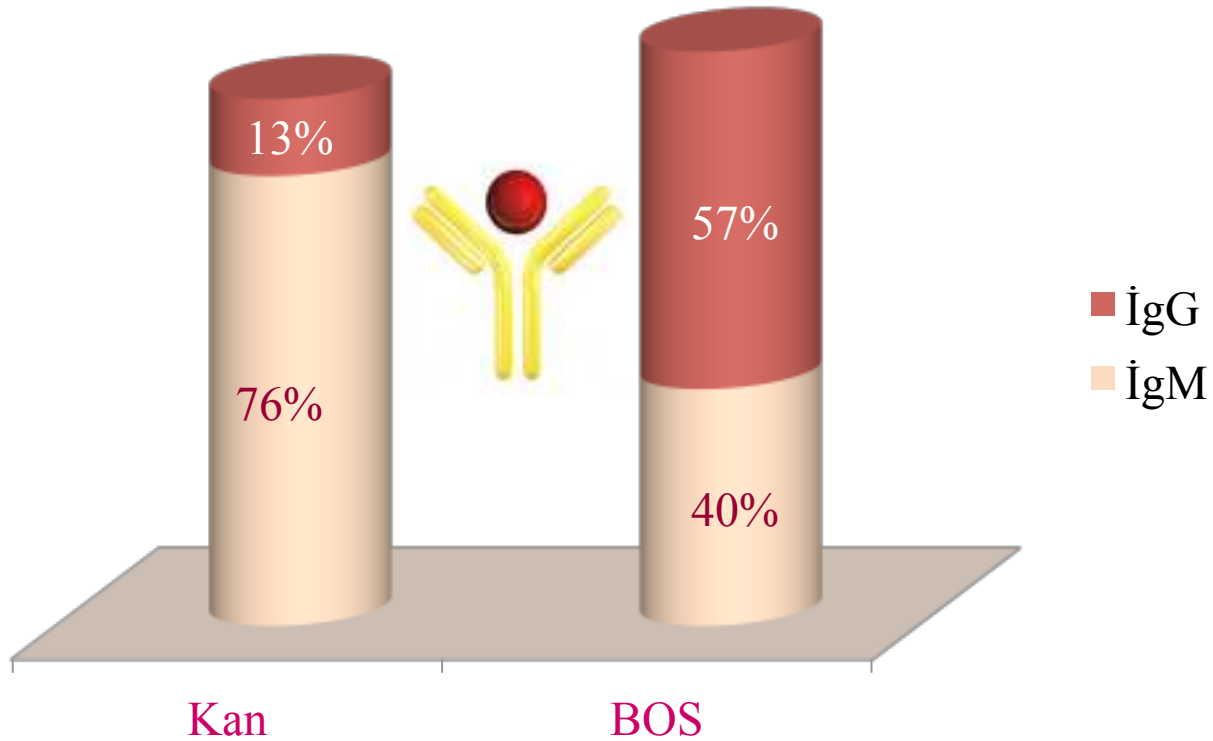
Kontrol LP, PCR

- Tedavi ile altında, 7 gün
- Yaklaşık yarısı negatifleşiyor



Çağ Y, Erdem H, Leib S, et al. Managing atypical and typical Herpetic central nervous system infections: Results of a multinational study. Clinical Microbiology and Infection (Yayında).

Seroloji



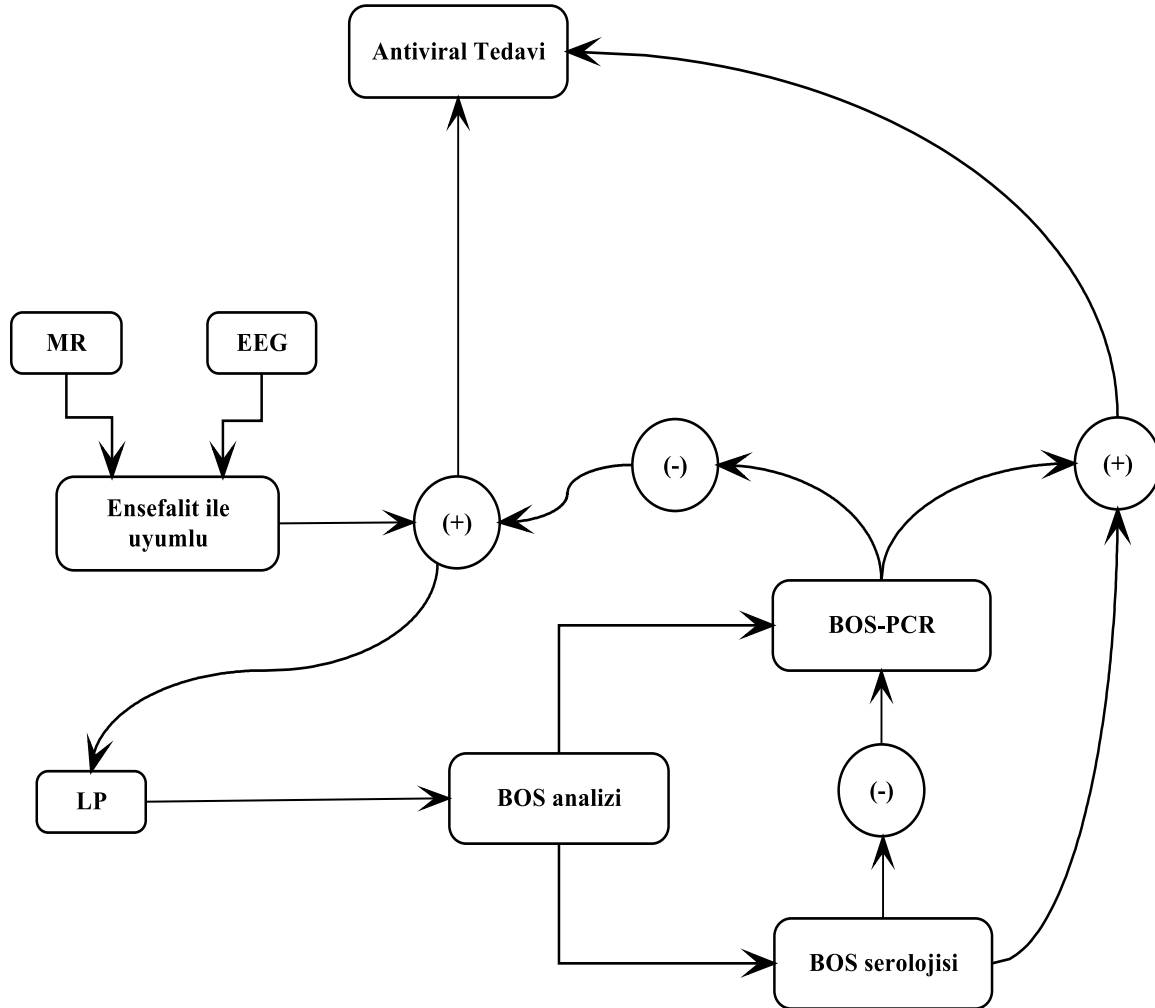
Çağ Y, Erdem H, Leib S, et al. Managing atypical and typical Herpetic central nervous system infections: Results of a multinational study. Clinical Microbiology and Infection (Yayında).

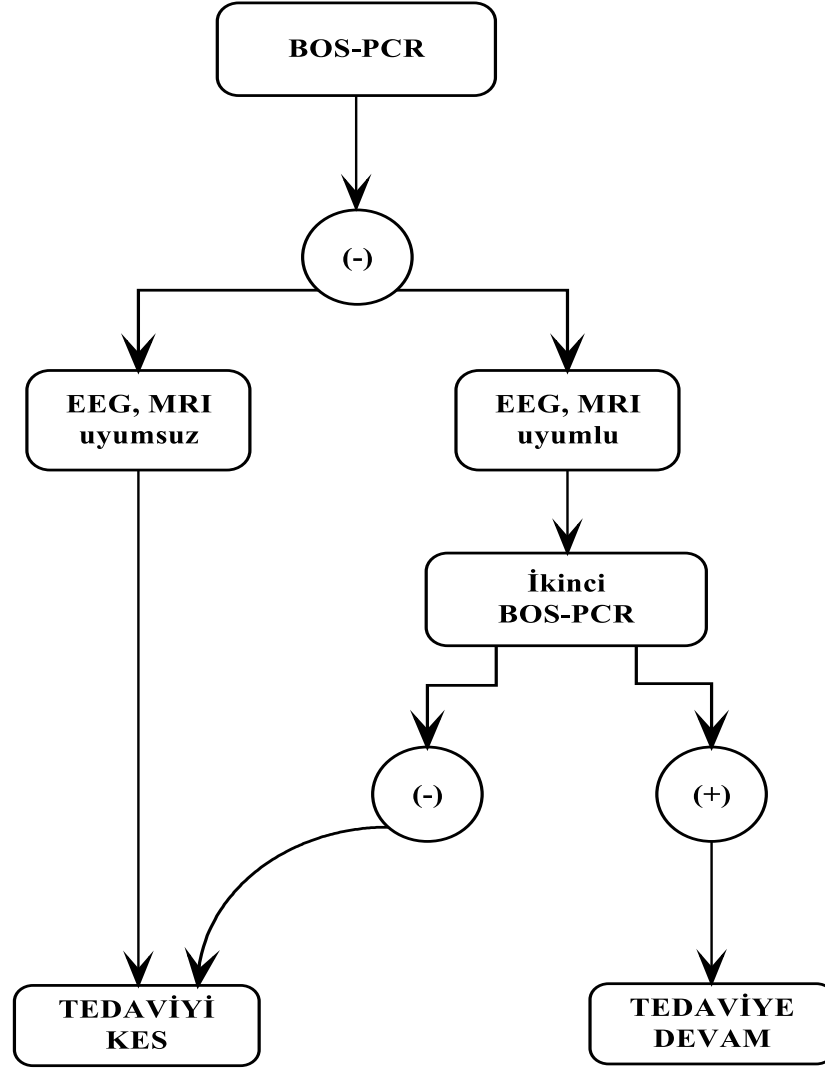
BOS HSV PCR

- Yanlış negatif sonuç
 - İlk 3-7 gün, tekrar?
 - Kanlı örnekler



- *Tunkel AR, et al. The management of encephalitis: Clinical practice guidelines by the infectious diseases society of America. Clinical infectious diseases an official publication of the IDSA. 2008; 47: 303-327.*
- *Machado Ldos R, et al. CSF analysis in infectious diseases of the nervous system: When to ask, what to ask, what to expect. Arquivos de neuropsiquiatria. 2013; 71: 693-698.*
- *Sauerbrei A, Wutzler P. Laboratory diagnosis of central nervous system infections caused by herpesviruses. Journal of clinical virology . 2002; 25 Suppl 1: S45-51.*
- *Bhullar SS, et al. Determination of viral load by quantitative RT-PCR in HSV encephalitis patients. Intervirology. 2014; 57: 1-7.*





Güncel Rehber

Major Kriterler

- ≥ 24 saati aşan şuur değişikliği
 - Şuur düzeyinde ↘
 - Letarji
 - Kişilik değişiklikleri



Minör Kriterler

- 2 olası, ≥ 3 muhtemel
 - Ateş $\geq 38^{\circ}$ C
 - BOS $\geq 5/\text{mm}^3$ lökosit
 - Konvülziyonlar
 - Yeni başlayan fokal tutulum
 - Kranial inceleme uyumlu (MR)
 - Uyumlu EEG bulguları

Güncel IDSA Rehberi-2

Şuur deęişiklięi

- İleri menenjitlerde de (+)



Minör parametreler

- Ateş $\geq 38^{\circ}$ C
- BOS $\geq 5/\text{mm}^3$ lökosit
- Konvülziyonlar
- Yeni başlayan fokal nörolojik kayıp

Teşekkürler...



✉ hakanerdem1969@yahoo.com