

**Ελληνική Γαστρεντερολογική Εταιρεία, Τμήμα Βορείου Ελλάδας
Επιστημονική Εκπαιδευτική Διημερίδα**

Αποφασίζοντας την πρώτη επιλογή θεραπείας στα ΙΦΝΕ

***Κωνσταντίνος Σουφλέρης
Γαστρεντερολόγος, Επιμελητής Α' Ε.Σ.Υ.
Γαστρεντερολογική Κλινική
«Θεαγένειο» Α.Ν.Θ.
Θεσσαλονίκη***



6 Οκτωβρίου 2018, Ολυμπιακό Μουσείο Θεσσαλονίκης

ΔΗΛΩΣΗ ΣΥΓΚΡΟΥΣΗΣ ΣΥΜΦΕΡΟΝΤΩΝ (Disclosures)

Abbvie (Humira)

Τιμητικές Αμοιβές, Ταξιδιωτικές Χορηγίες

Aenorasis (Inflectra)

Τιμητικές Αμοιβές, Ταξιδιωτικές Χορηγίες

Janssen (Stelara)

Τιμητικές Αμοιβές

Merck (Remicade, Simponi)

Τιμητικές Αμοιβές, Ταξιδιωτικές Χορηγίες

Pfizer (Xeljanz)*

Τιμητικές Αμοιβές

Takeda (Entyvio)

Τιμητικές Αμοιβές, Ταξιδιωτικές Χορηγίες

Νόσος του Crohn-Βιολογικές Θεραπείες

- **Infliximab-1998**
- **Adalimumab-2007**
- **Vedolizumab-2014**
- **Ustekinumab-2016**

Ελκώδης Κολίτιδα-Βιολογικές Θεραπείες

- **Infliximab-2005**
- **Adalimumab-2012**
- **Golimumab-2013**
- **Vedolizumab-2014**
- **Tofacitinib-2019***

Νόσος του Crohn



American College of Gastroenterology
Digestive Disease Specialists Committed to Quality
in Patient Care

24. **Anti-TNF agents** (infliximab, adalimumab) should be used to treat Crohn's disease that is **resistant to treatment with corticosteroids** (strong recommendation, moderate level of evidence)...
25. **Anti-TNF agents** should be given for Crohn's disease **refractory to thiopurines or methotrexate** (strong recommendation, moderate level of evidence)...
27. For patients with **moderately to severely active Crohn's disease and objective evidence of active disease**, anti-integrin therapy (with **vedolizumab**) with or without an immunomodulator is more effective than placebo and should be considered to be used for induction of symptomatic remission in patients with Crohn's disease (strong recommendation, high level of evidence)...
30. **Ustekinumab** should be given for **moderate-to-severe Crohn's disease patients who failed previous treatment with corticosteroids, thiopurines, methotrexate, or anti-TNF inhibitors or who have had no prior exposure to anti-TNF inhibitors** (strong recommendation, high level of evidence)...

Νόσος του Crohn



American College of Gastroenterology
Digestive Disease Specialists Committed to Quality
in Patient Care

- 33. **Anti-TNF agents** (infliximab, adalimumab) can be considered to treat **severely active Crohn's disease** (strong recommendation, moderate level of evidence)...
- 34. **Infliximab** may be administered to treat **fulminant Crohn's disease** (conditional recommendation, low level of evidence)...
- 35. **Infliximab** is effective and should be considered in treating **perianal fistulas** in Crohn's disease (strong recommendation, moderate level of evidence)...
- 36. **Infliximab** may be effective and should be considered in treating **enterocutaneous and rectovaginal fistulas** (strong recommendation, moderate level of evidence)...
- 37. **Adalimumab** may be effective and should be considered in treating **perianal fistulas** (strong recommendation, low level of evidence)...
- 58. In **high-risk** patients, **anti-TNF agents** should be started within 4 weeks of surgery in order **to prevent postoperative Crohn's disease recurrence** (conditional recommendation, low level of evidence)...

Ελκώδης Κολίτιδα



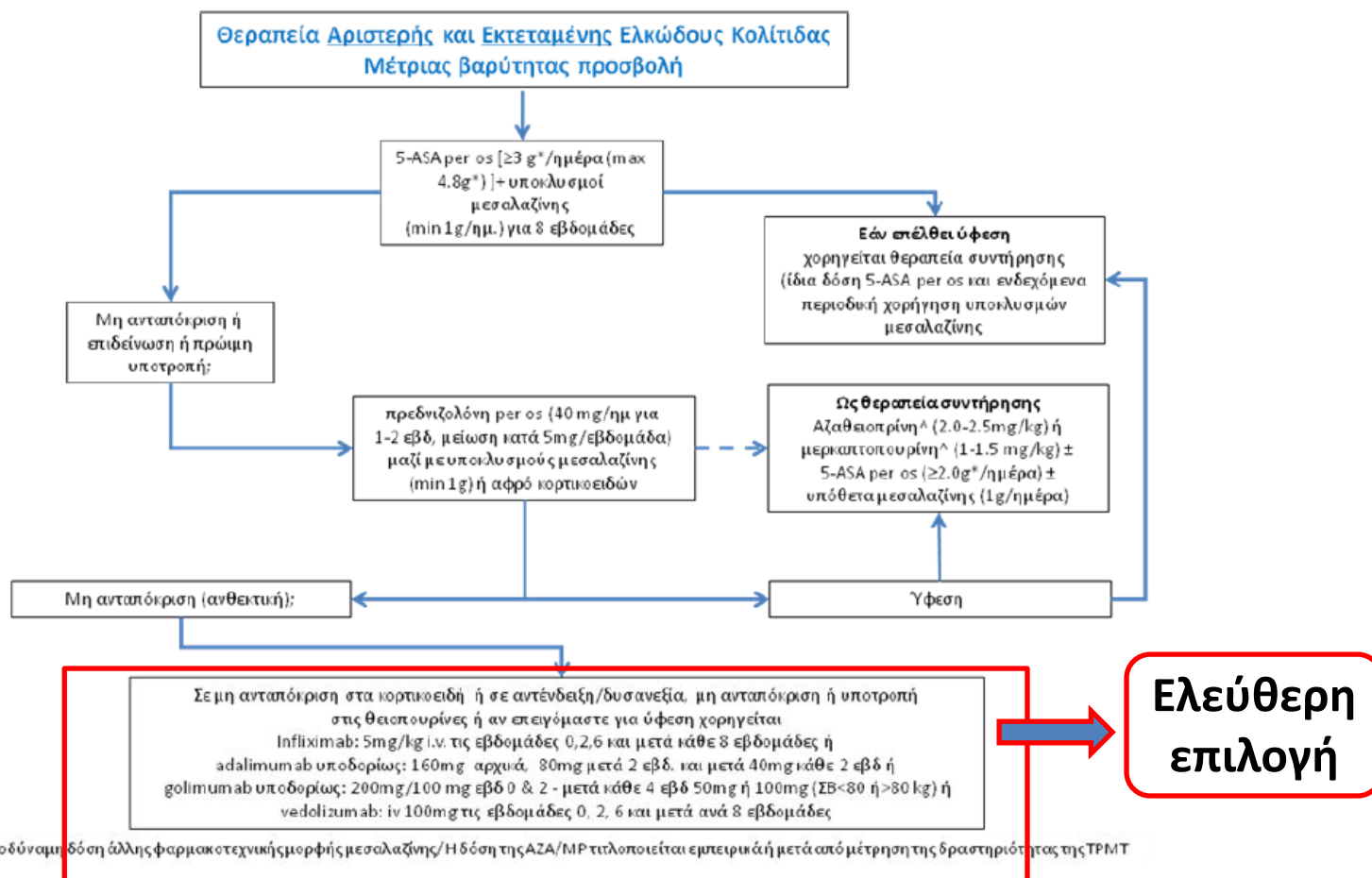
11I. Patients with **steroid-dependent disease** should be treated with a thiopurine [EL2], anti-TNF [EL1] [preferably combined with thiopurines, at least for infliximab [EL2]], vedolizumab [EL2], or methotrexate [EL2]...

11J. **Moderate disease refractory to oral steroids** should be treated either with Intravenous steroids [EL4] or anti-TNF [EL1] preferably combined with thiopurines, at least for infliximab [EL2], vedolizumab [EL2], or tacrolimus [EL2]...

11K. Patients with **moderate colitis refractory to thiopurines** should be treated with anti TNF [EL1], preferably combined with thiopurines, at least for infliximab [EL2], or vedolizumab [EL2]...

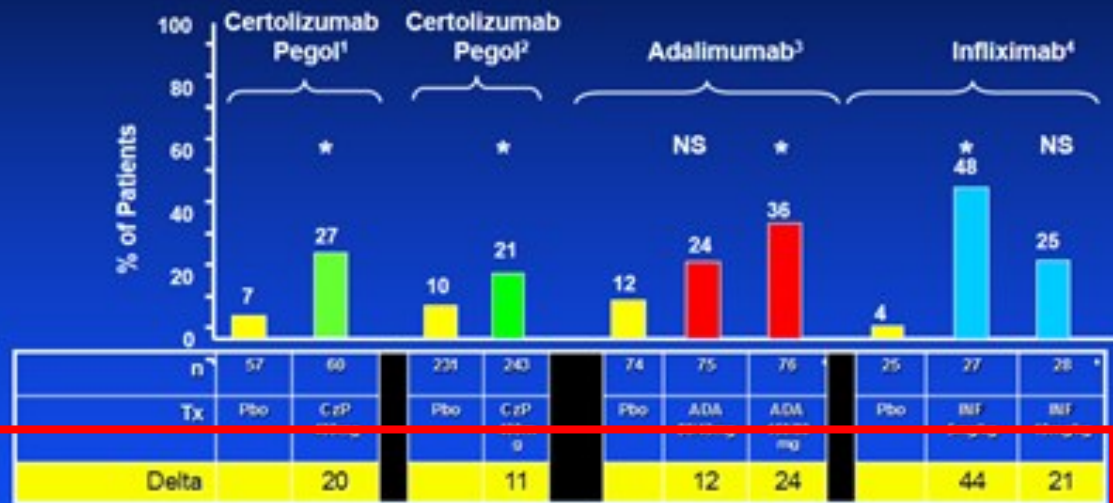
11H. The response **to intravenous steroids** should be best assessed by the third day [EL3]; In **non-responders**, treatment options including ciclosporin [EL1], infliximab [EL1], tacrolimus [EL2], or surgery should be considered...

Ελλάδα: Θεραπευτικά Πρωτόκολλα και ΙΦΝΕ Ελκώδης Κολίτιδα



Σύγκριση μεταξύ των αντι TNF σε νόσο του Crohn

Induction of Clinical Remission at Week 4 In Crohn's Disease: Certolizumab, Adalimumab, Infliximab



1. Schreiber et al. Gastroenterology. 2005 Sep;129(3):807-18

2. Sandborn et al. N Engl J Med 2007

3. Hanauer et al. Gastroenterology 2006;130:323-333

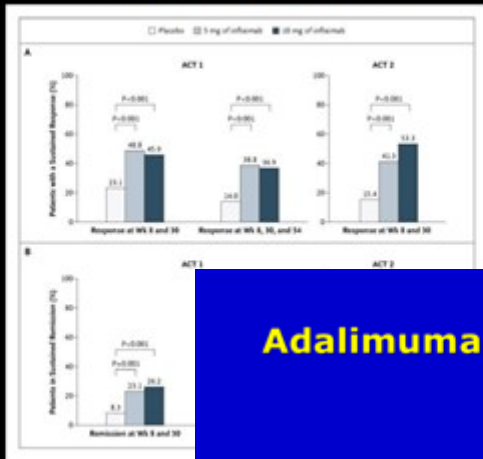
4. Targan et al. N Engl J Med 1997;337:1029-1035

* p<0.05

NS Non-significance

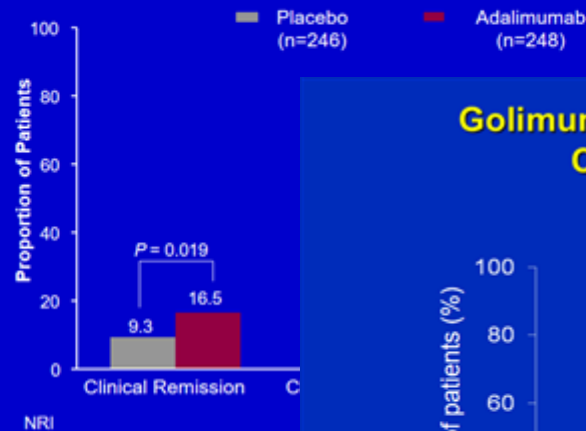
Anti TNF στην Ελκώδη Κολίτιδα

Proportion of Patients with a Sustained Clinical Response (Panel A) and in Sustained Clinical Remission (Panel B) in ACT 1 and ACT 2

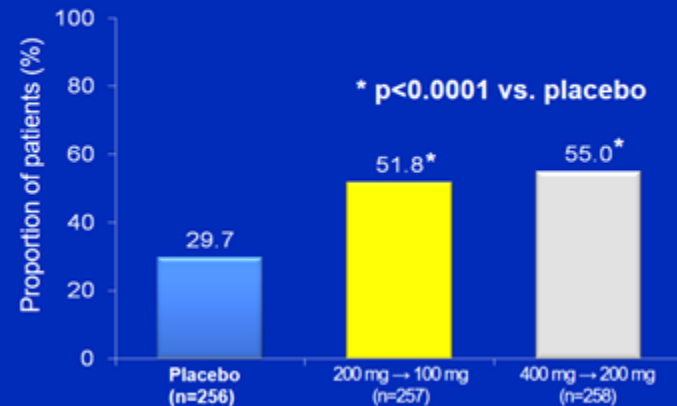


Rutgeerts P, Sandborn WJ, et al. N Engl J Med 2005;353:2462-2476

Adalimumab Induction for Ulcerative Colitis Results at Week 8



Golimumab Induction for Ulcerative Colitis Clinical Response† at Week 6

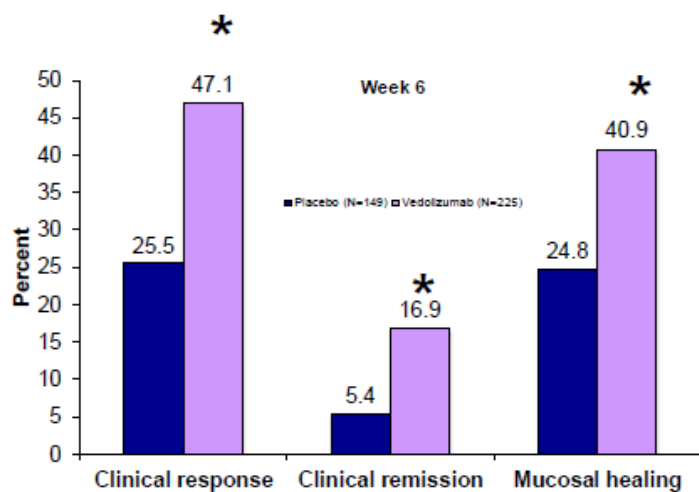


Sandborn W. Gastroenterology 2014

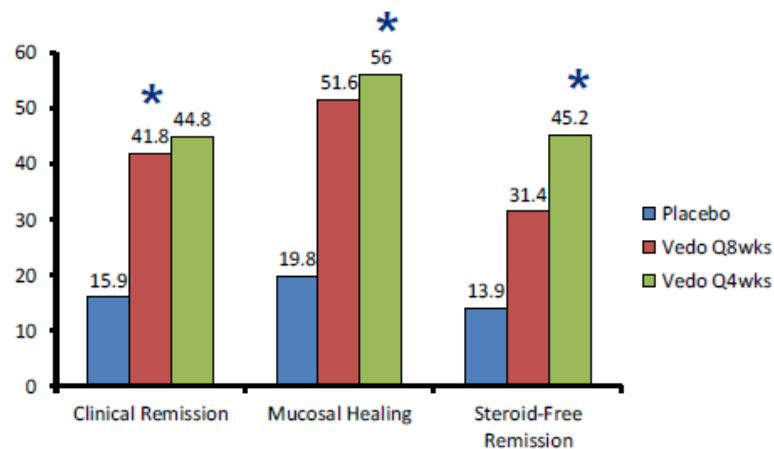
† Defined as a decrease from baseline in the Mayo score by $\geq 30\%$ and ≥ 3 points, with either a decrease from baseline in the rectal bleeding subscore of ≥ 1 or a rectal bleeding subscore of 0 or 1

Vedolizumab-Ελκώδης Κολίτιδα

GEMINI 1



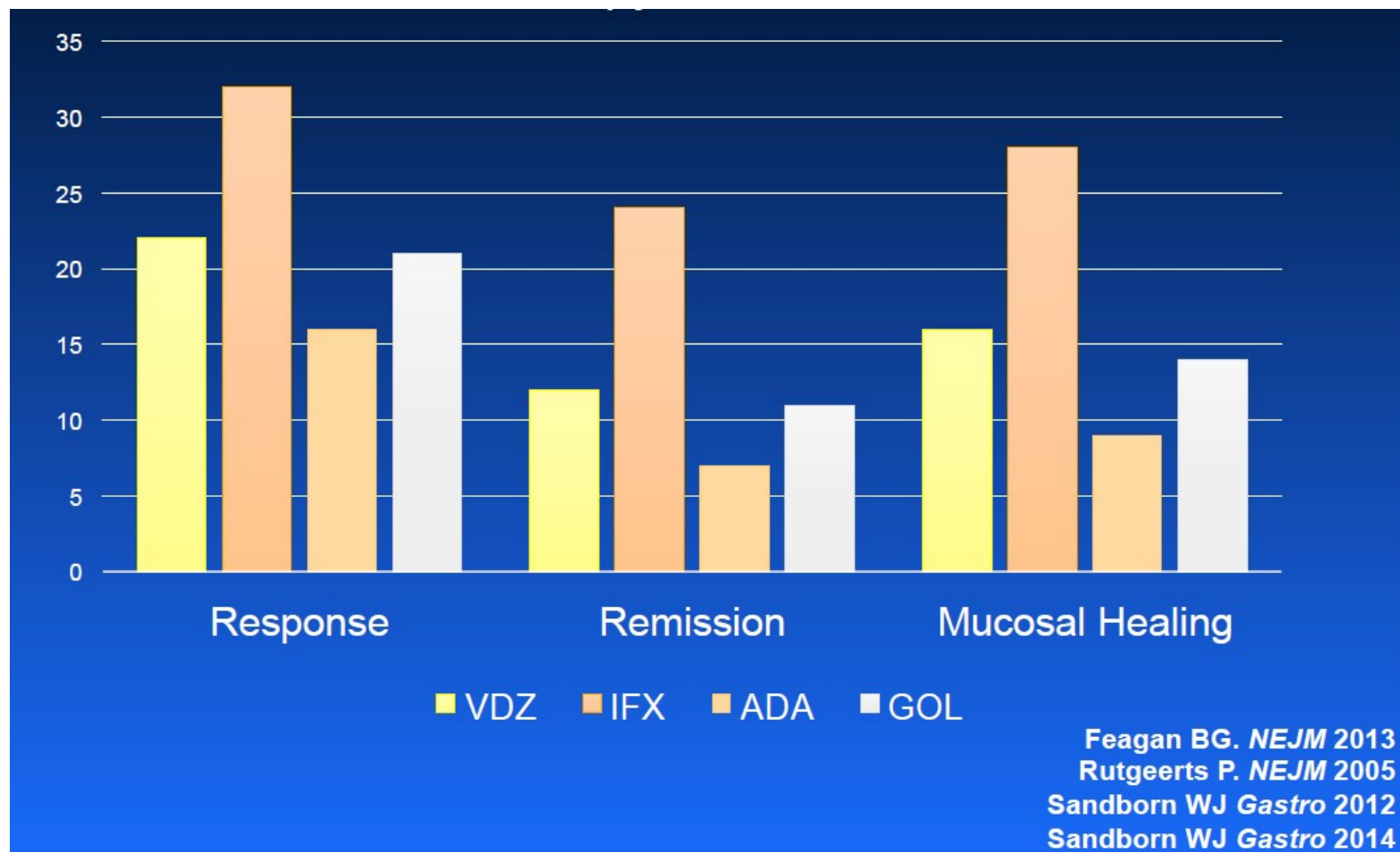
* p<0.001



Randomized responders
Week 52

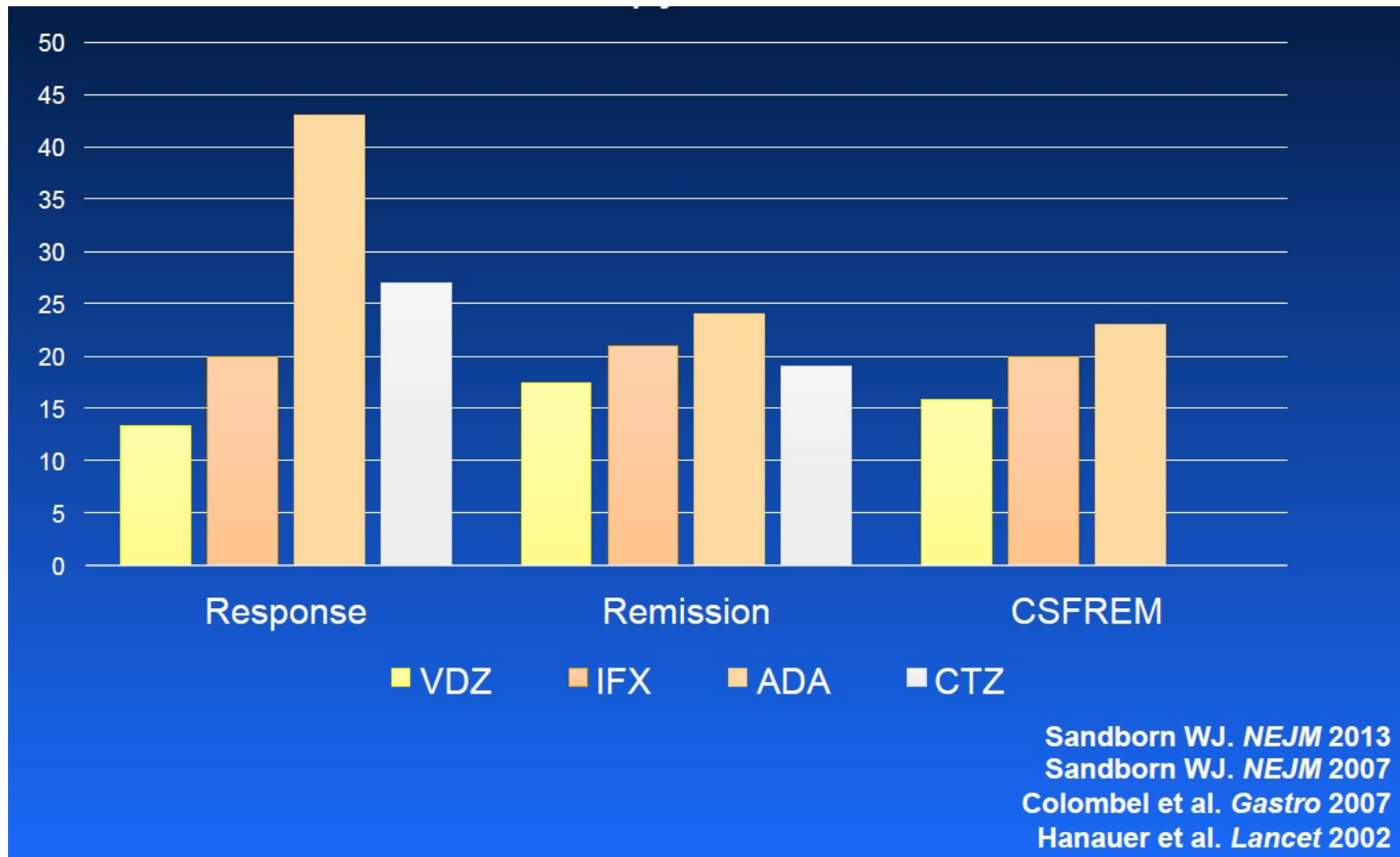
Ελκώδης Κολίτιδα και Βιολογικές Θεραπείες

Induction incremental benefits (Deltas)

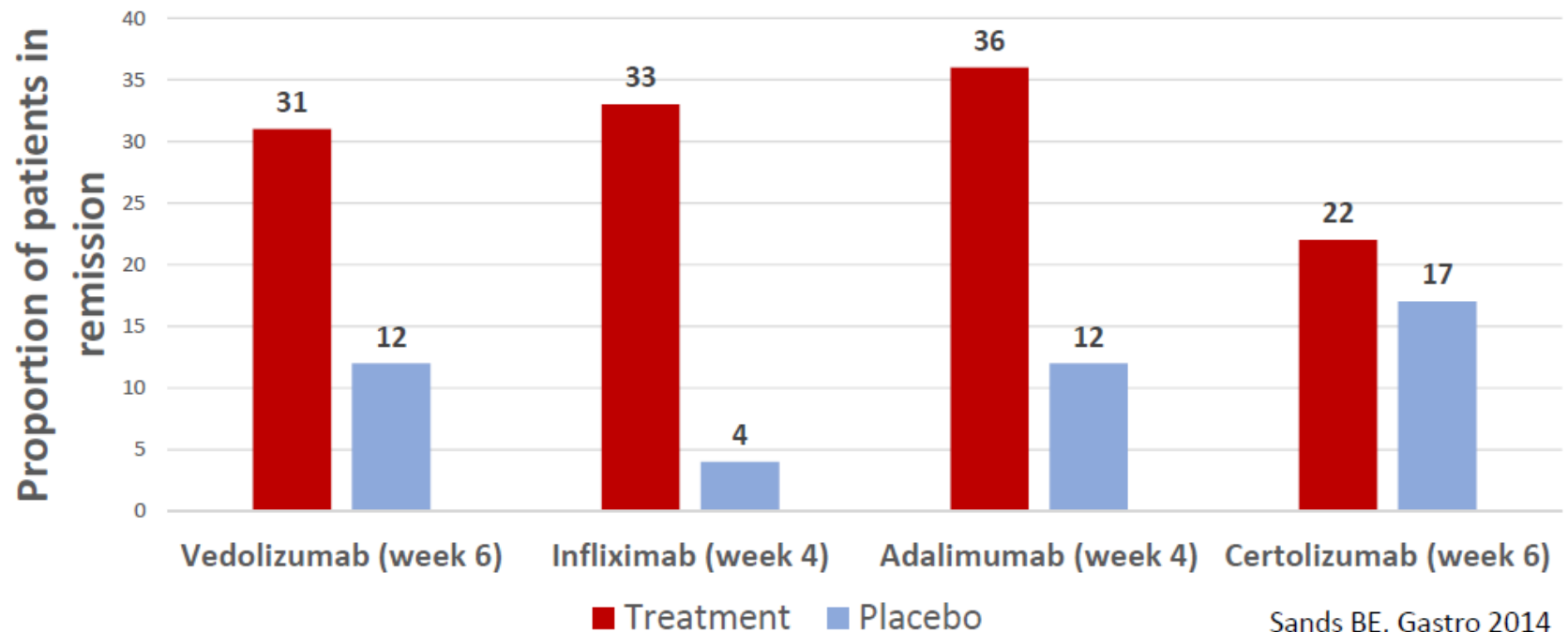


Νόσος του Crohn και Βιολογικές Θεραπείες

Induction incremental benefits (Deltas)



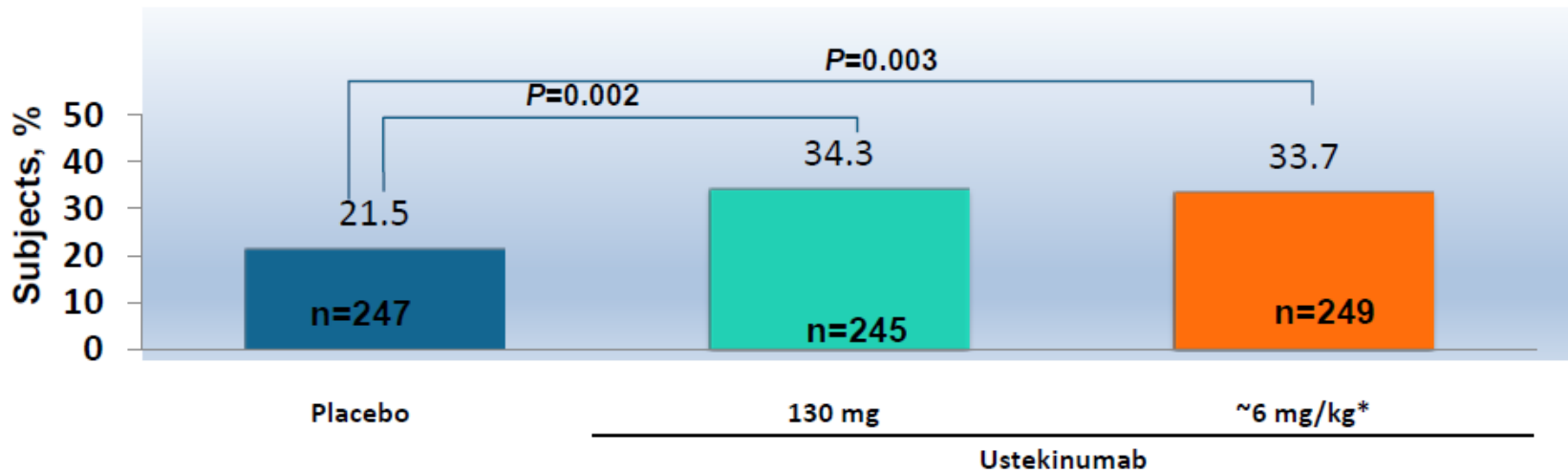
Induction σε naïve ασθενείς με νόσο του Crohn διαφορές βιολογικών θεραπειών;



Sands BE, Gastro 2014
Targan SR, NEJM 1997
Hanauer SB, Gastro 2006
Sandborn WJ, NEJM 2007

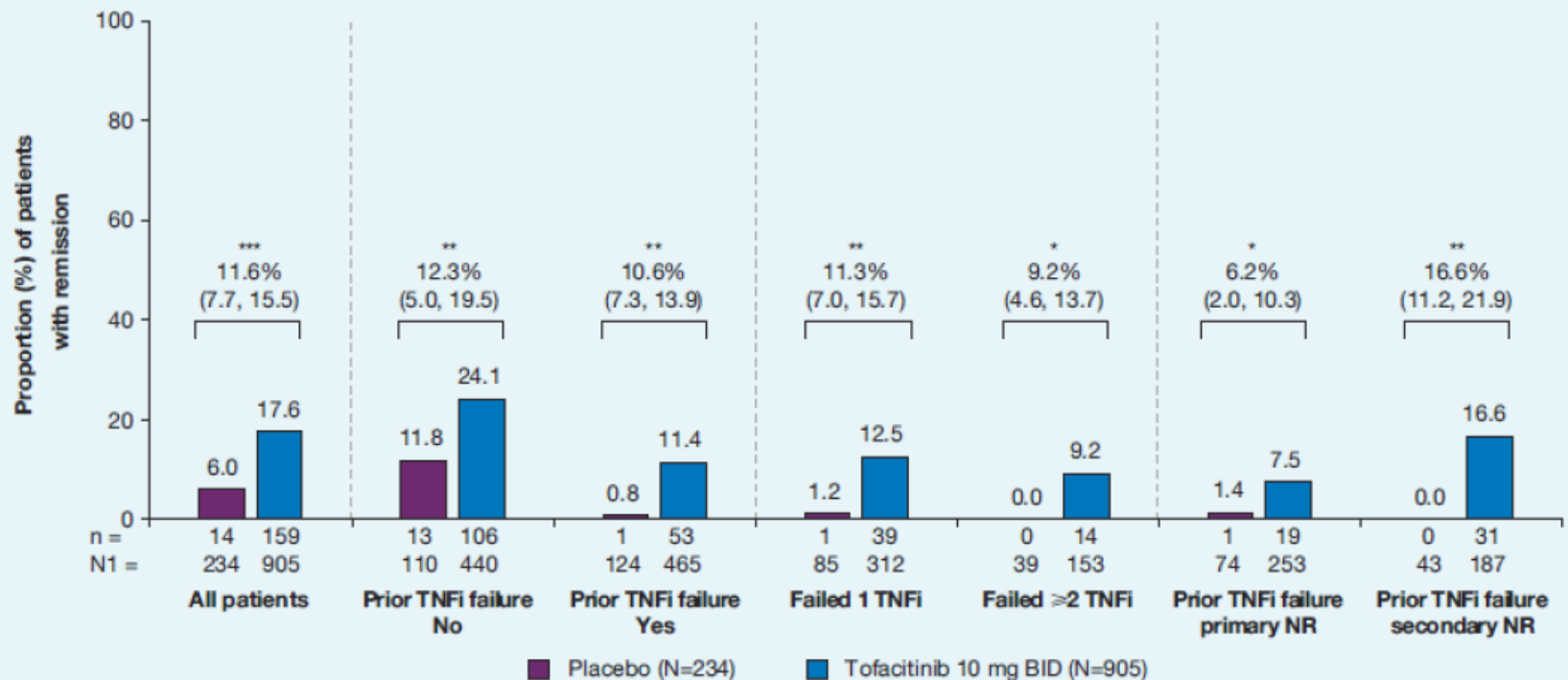
Ustekinumab σε νόσο του Crohn

Clinical Response at Week 6 (≥ 100 point CDAI reduction)



Tofacitinib

a) Patients in remission at Week 8 in OCTAVE Induction 1 and 2



Σύγκριση Βιολογικών Θεραπειών και Κλινικές Μελέτες

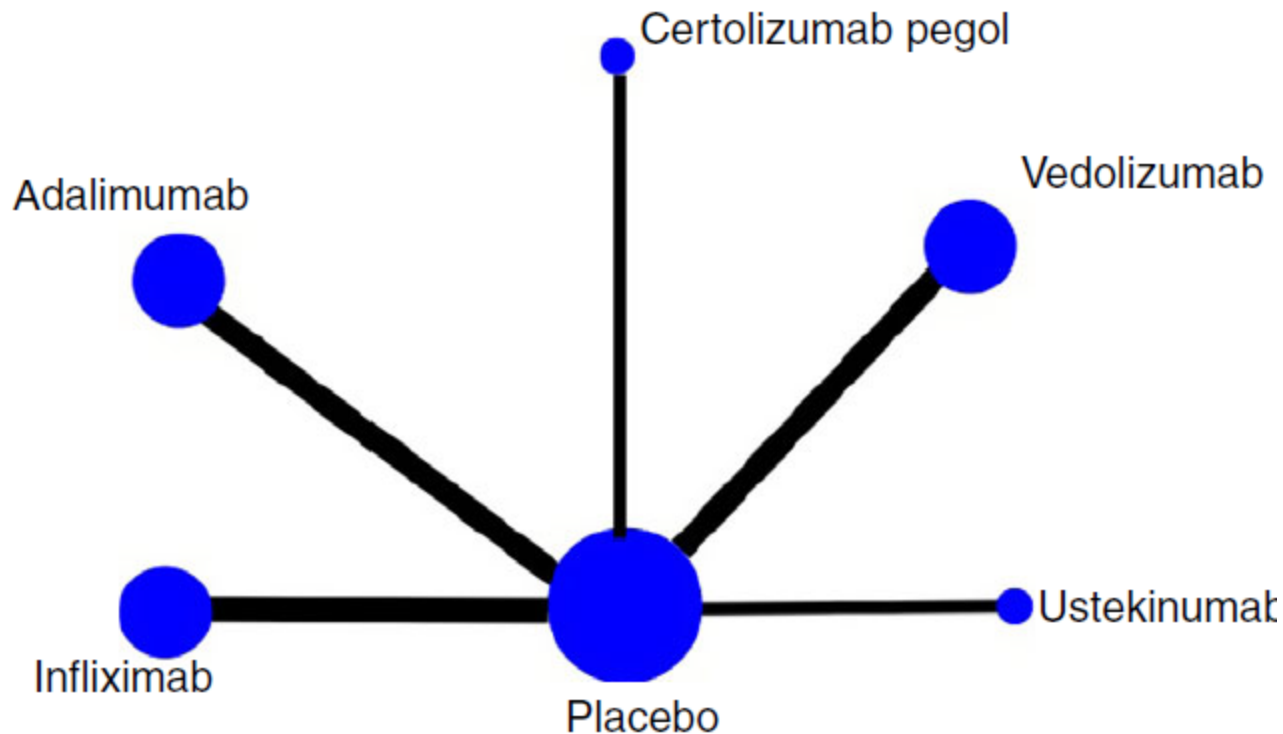
- Δεν υπάρχουν Head to Head μελέτες
- **Comparative Effectiveness Research (CER)**-Ετερογένεια
 - study time-points
 - prior anti-TNF exposure
 - study populations
 - study endpoints
 - large placebo effect
 - dosing
- Νέες μελέτες
 - placebo;
 - superiority; (σύγκριση με πολύ αποτελεσματική θεραπεία-anti TNF)
 - non inferiority (inferiority margin)

better/? Safer? Easier? Cheaper?

Βιολογικές Θεραπείες και Νόσος του Crohn

Network Meta-analysis

8 RTCs, 1458 pts



Βιολογικές Θεραπείες σε bio-naïve ασθενείς με νόσο του Crohn

Επαγωγή Ύφεσης

• Placebo	20,0%
• Infliximab	59,6%
• Adalimumab	48,7%
• Ustekinumab	40,7%
• Vedolizumab	40,2%

SUCRA

Surface Under the Cumulative Ranking

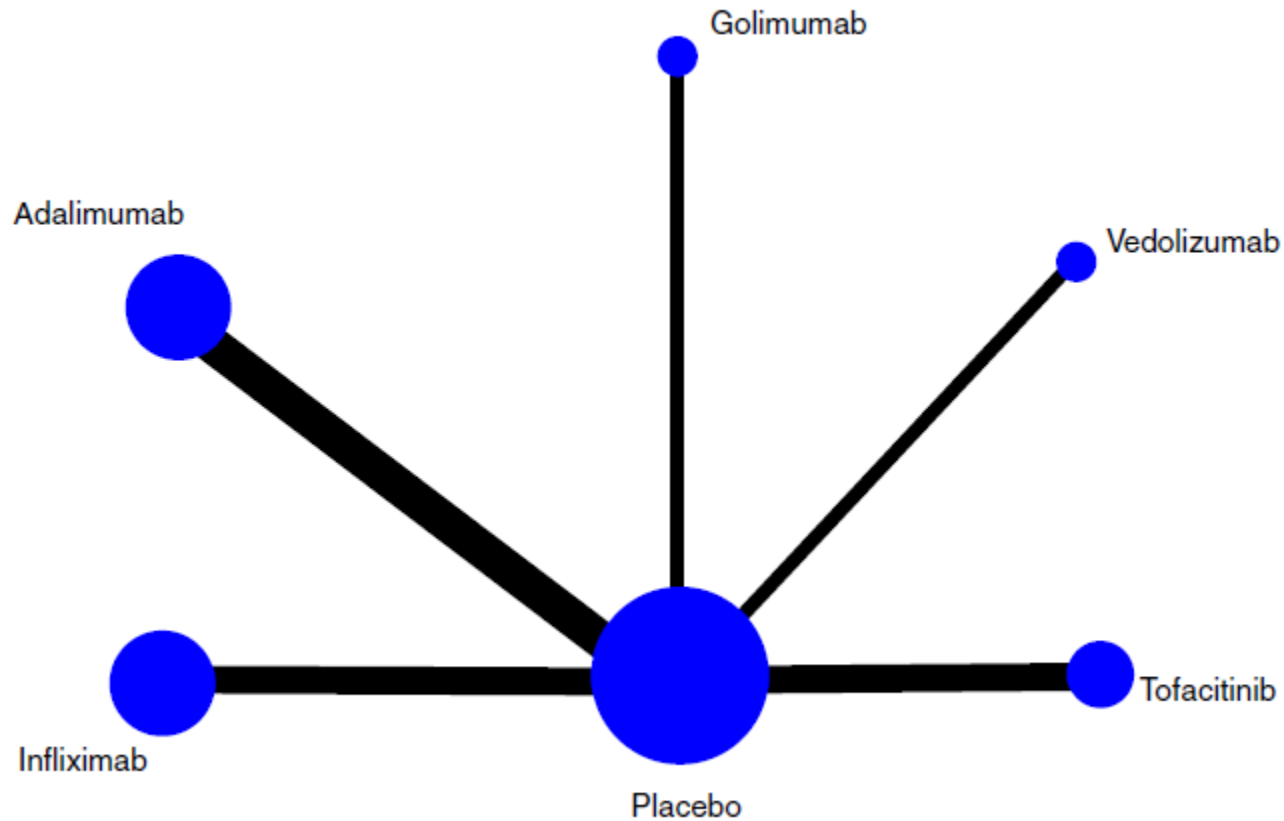
• Infliximab	0,90
• Adalimumab	0,75
• Ustekinumab	0,56
• Vedolizumab	0,55

Maintenance: Adalimumab, Infliximab, 2nd line: Ustekinumab (adalimumab if LOR)

Βιολογικές Θεραπείες και Ελκώδης Κολίτιδα

Network Meta-analysis

12 RCTs, 2720 patients



Βιολογικές Θεραπείες σε bio-naïve ασθενείς με Ελκώδη Κολίτιδα

Επαγωγή Ύφεσης Remission %

• Placebo	9,81%
• Infliximab	30,9%
• Vedolizumab	31,6%
• Golimumab	23,0%
• Tofacitinib	18,9%
• Adalimumab	16,1%

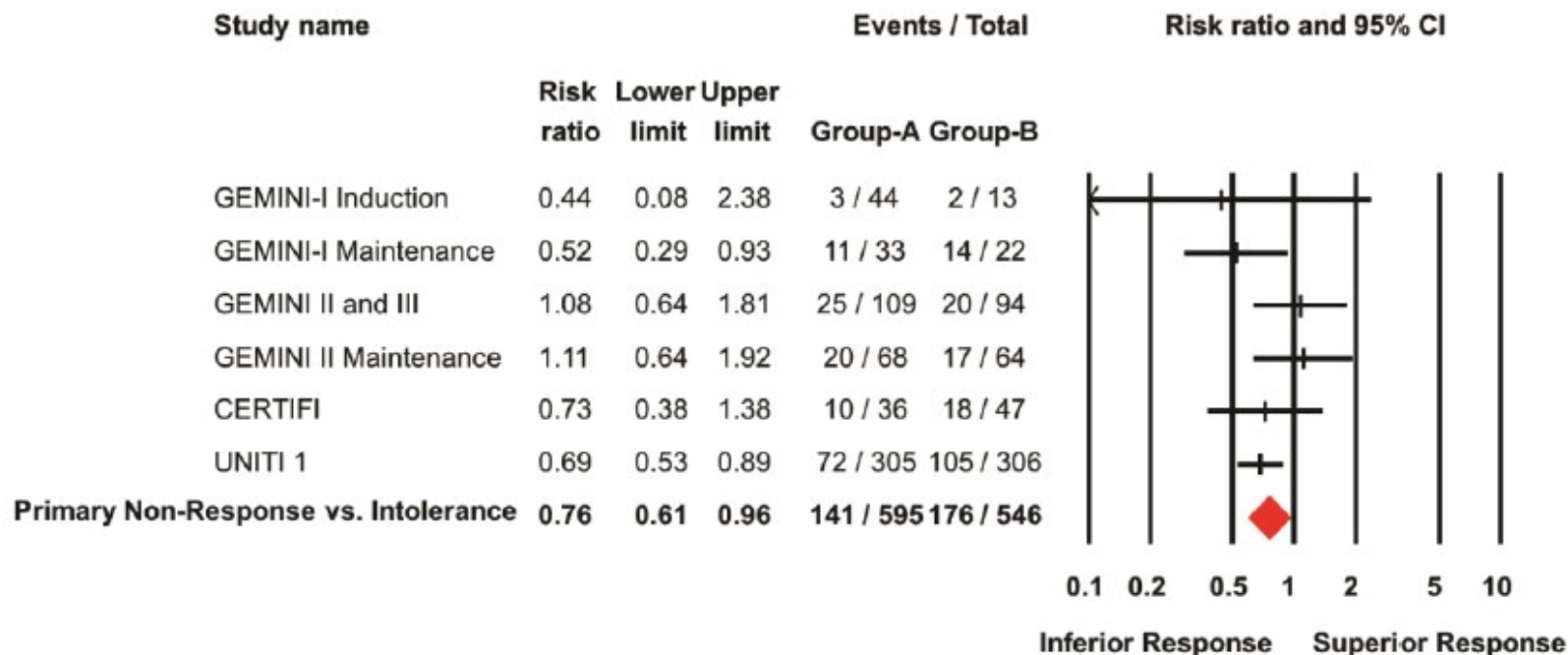
SUCRA Surface Under the Cumulative Ranking

• Infliximab	0,85
• Vedolizumab	0,82
• Golimumab	0,58
• Tofacitinib	0,43
• Adalimumab	0,31

2nd Line SUCRAs: tofacitinib 0.96, vedolizumab 0.62, adalimumab 0.31

PNR versus LOR/Intolerance to anti-TNF: 27% μικρότερη ανταπόκριση σε 2^{ης} γραμμής βιολογική θεραπεία

Response to Second-line Biologics - Prior PNR vs. Intolerance



Anti-TNFs-Τοξικότητα

- Ανοσογονικότητα
- Αντιδράσεις στην έγχυση (infliximab)
- Αντιδράσεις καθυστερημένης υπερευασθησίας (infliximab)
- Τοπικές αντιδράσεις στο σημείο της έγχυσης (adalimumab, golimumab)
- Αυτο-αντισώματα (κυρίως infliximab, λιγότερο adalimumab)
- Φαρμακευτικός Λύκος
- Non Hodgkin Λέμφωμα (και το ηπατοσπληνικό λέμφωμα σε νεαρή ηλικία με infliximab ή adalimumab και αζαθιοπρίνη)
- Σοβαρές Λοιμώξεις
- Ευκαιριακές Λοιμώξεις (φυματίωση, ιστοπλάσμωση)
- Απομυελινωτική Νόσος

Anti-TNF και Κίνδυνος για Σοβαρές Λοιμώξεις

Anti-TNF Monotherapy, Combination Therapy, Thiopurines

Table 3. Multivariable Adjusted HRs (95% CIs)^a of Serious Infections According to Medication Exposure, Overall and by Infection Site

Type of Infection	Exposed to Combination Therapy vs Anti-TNF Monotherapy	Exposed to Combination Therapy vs Thiopurine Monotherapy	Exposed to Anti-TNF Monotherapy vs Thiopurine Monotherapy
Serious infections, overall	1.23 (1.05–1.45)	2.11 (1.80–2.48)	1.71 (1.56–1.88)
Pulmonary infections	1.40 (0.99–1.98)	3.14 (2.24–4.40)	2.24 (1.83–2.75)
GI infections	1.34 (0.93–1.93)	1.84 (1.30–2.60)	1.37 (1.12–1.68)
Skin infections	1.08 (0.76–1.54)	1.86 (1.30–2.68)	1.72 (1.38–2.15)
Urinary tract infections	0.89 (0.56–1.41)	1.69 (1.07–2.67)	1.90 (1.47–2.45)
ENT infections	1.47 (0.60–3.59)	1.95 (0.80–4.73)	1.32 (0.83–2.12)
Musculoskeletal infections	1.89 (0.78–4.55)	2.58 (1.07–6.23)	1.36 (0.68–2.73)
Other infections	1.26 (0.89–1.79)	2.03 (1.44–2.87)	1.61 (1.29–2.01)

Anti-TNF vs Thiopurines: X 1.7

Unexposed: 8,4/1,000 patient/years

Thiopurines Monotherapy: 10,5/1,000 patient/years

RR:1,3

Anti-TNF Monotherapy: 18,9/1,000 patient/years

RR:2,3

Combination Therapy: 22,4/1,000 patient/years

RR:2,8

Anti-TNF και Κίνδυνος για Ευκαιριακές Λοιμώξεις

Anti-TNF Monotherapy, Combination Therapy, Thiopurines

Table 4. Multivariable Adjusted HRs (95% CIs)^a of Opportunistic Infections According to Medication Exposure, Overall and by Pathogen

Type of Infection	Exposed to Combination Therapy vs Anti-TNF Monotherapy	Exposed to Combination Therapy vs Thiopurine Monotherapy	Exposed to Anti-TNF Monotherapy vs Thiopurine Monotherapy
Opportunistic infections, overall	1.96 (1.32–2.91)	2.11 (1.45–3.08)	1.08 (0.83–1.40)
Viral infections	1.98 (1.00–3.94)	1.13 (0.62–2.08)	0.57 (0.38–0.87)
Mycobacterial infections	2.17 (1.08–4.36)	4.30 (2.10–8.80)	1.98 (1.15–3.40)
Bacterial infections	1.99 (0.99–4.01)	4.73 (2.10–10.7)	2.38 (1.23–4.58)
Fungal infections	0.78 (0.21–2.88)	0.96 (0.26–3.61)	1.24 (0.49–3.16)

- Anti TNF αυξάνουν τον κίνδυνο για ευκαιριακές λοιμώξεις (Tbc, Bacteria)
- Θιοπουρίνες αυξάνουν τον κίνδυνο για ιογενείς ευκαιριακές λοιμώξεις

Anti-TNF και Κίνδυνος για Λέμφωμα

Anti-TNF Monotherapy, Combination Therapy, Thiopurines

Table 2. Incidence of Lymphoma According to Exposure Group

Lymphoma Type	Overall (1 060 336 PY)		Unexposed to Thiopurines or Anti-TNF Agents (838 611 PY)		Exposed to Thiopurine Monotherapy (129 743 PY)		Exposed to Anti-TNF Monotherapy (77 229 PY)		Exposed to Combination Therapy (14 753 PY)	
	No. of Events	IR per 1000 PY (95% CI)	No. of Events	IR per 1000 PY (95% CI)	No. of Events	IR per 1000 PY (95% CI)	No. of Events	IR per 1000 PY (95% CI)	No. of Events	IR per 1000 PY (95% CI)
All Patients										
All lymphoma	336	0.32 (0.28-0.35)	220	0.26 (0.23-0.29)	70	0.54 (0.41-0.67)	32	0.41 (0.27-0.55)	14	0.95 (0.45-1.45)
Hodgkin lymphoma	55	0.05 (0.04-0.07)	30	0.03 (0.02-0.04)	13	0.10 (0.05-0.15)	6	0.08 (0.02-0.14)	6	0.41 (0.08-0.74)
Non-Hodgkin lymphoma	281	0.27 (0.21-0.33)	190	0.23 (0.20-0.26)	57	0.44 (0.33-0.55)	26	0.34 (0.21-0.47)	8	0.54 (0.16-0.92)
Patients With Incident IBD^a										
All lymphoma	69	0.27 (0.21-0.33)	48	0.24 (0.17-0.31)	12	0.39 (0.17-0.61)	5	0.24 (0.03-0.45)	4	0.79 (0.01-1.57)
Hodgkin lymphoma	13	0.05 (0.02-0.08)	10	0.06 (0.03-0.09)	1	0.04 (0.0-0.10)	0	0	2	0.40 (0.0-0.95)
Non-Hodgkin lymphoma	56	0.22 (0.16-0.28)	38	0.19 (0.13-0.25)	11	0.36 (0.15-0.57)	5	0.24 (0.03-0.45)	2	0.40 (0.0-0.95)

Abbreviations: IBD, inflammatory bowel disease; IR, incidence rate; PY, person-years; TNF, tumor necrosis factor.

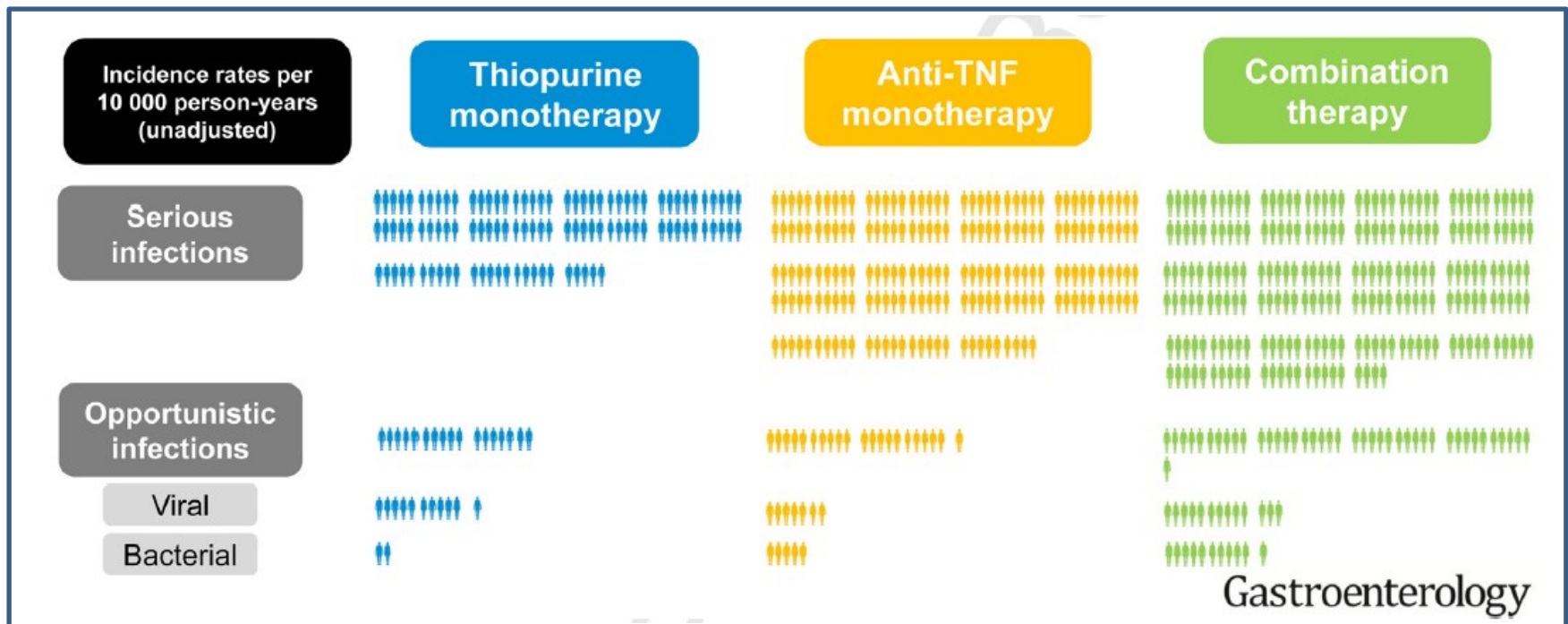
^a Patients with incident IBD account for 254 927 PY of follow-up overall: 198 555 as unexposed, 30 698 as exposed to thiopurine monotherapy, 20 637 as exposed to anti-TNF monotherapy, and 5037 as exposed to combination therapy.

Treatment	No thiopurine no IFX	Thiopurine mono	IFX mono	Combotherapy
Pts.yrs	522 487	111 113	60 736	11 514
Lymphoma n HR (IC ₉₅)	166	56 2.02 (1.08-2.26)	31 1.75 (1.15-3.03)	13 4.83 (2.51-9.16)

Lemaitre, JAMA 2017

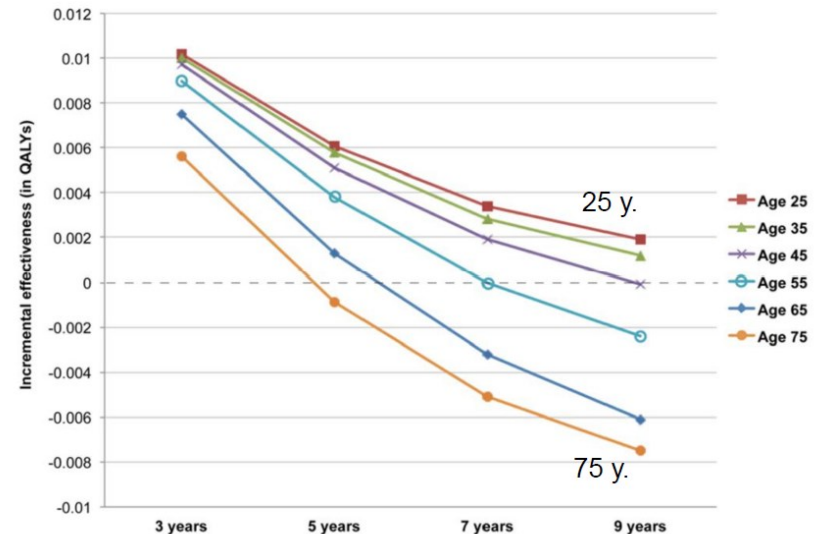
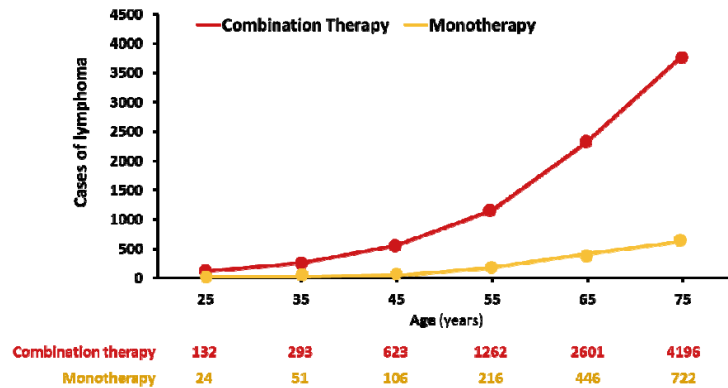
Anti-TNF και Κίνδυνος για Λοιμώξεις

Anti-TNF Monotherapy, Combination Therapy, Thiopurines



Ο κίνδυνος οφείλεται κυρίως στους anti-TNF

Anti-TNF (combo) και μεγάλη ηλικία: λιγότερη ασφάλεια αλλά και αποτελεσματικότητα



Vedolixumab και Ασφάλεια

- Πρόγραμμα Κλινικών Μελετών GEMINI

- χωρίς σημαντικά αυξημένο κίνδυνο σοβαρών λοιμώξεων

- κανένα περιστατικό PML

- παράγοντες κινδύνου για λοιμώξεις: στεροειδή, anti TNF αποτυχία

Colombel, Gut 2017

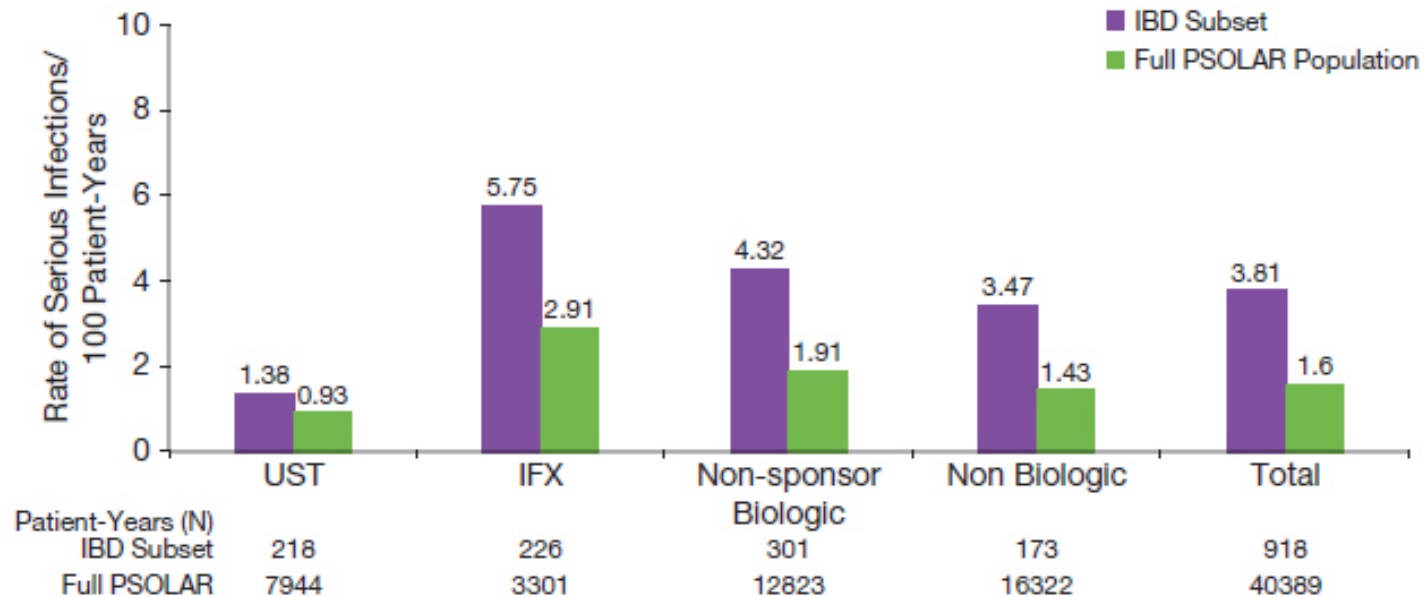
- **No black box warning**

- Περιεγχειρητική χρήση μάλλον ασφαλής

Lightner, JCC 2017

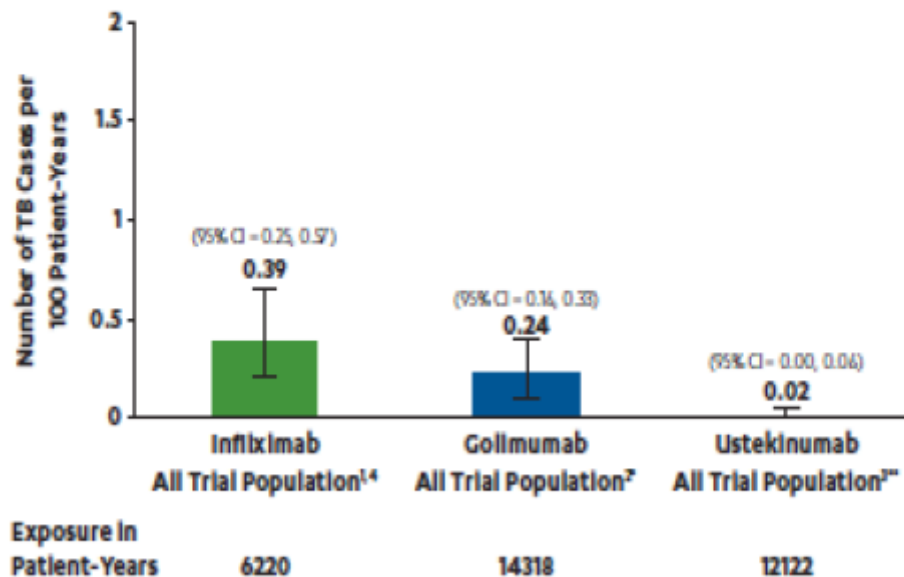
Ustekinumab και ασφάλεια

Figure 3. Rates of Serious Infections per 100 Patient-Years Within 91 Days of Biologic Administration

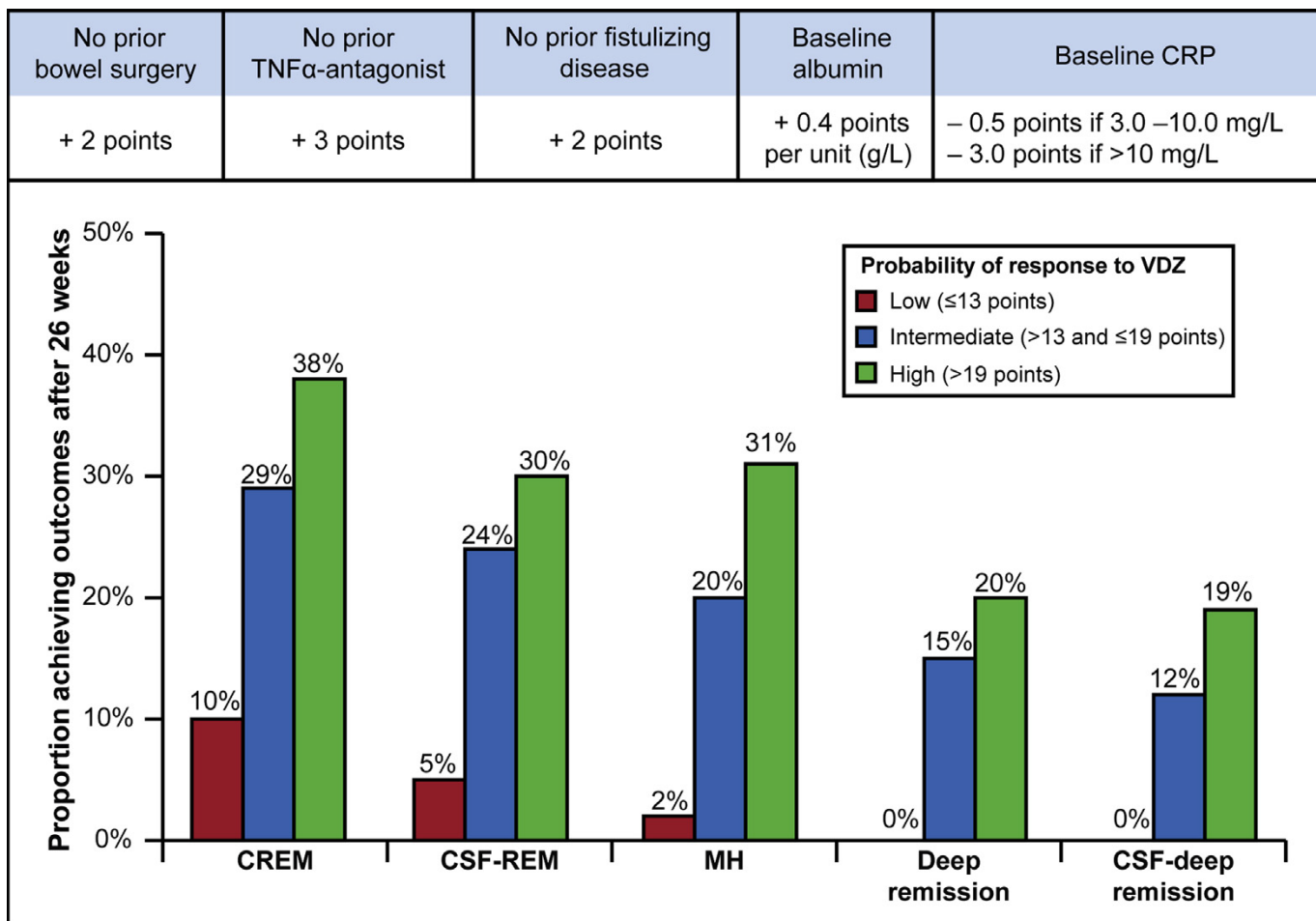


Βιολογικές Θεραπείες και Φυματίωση

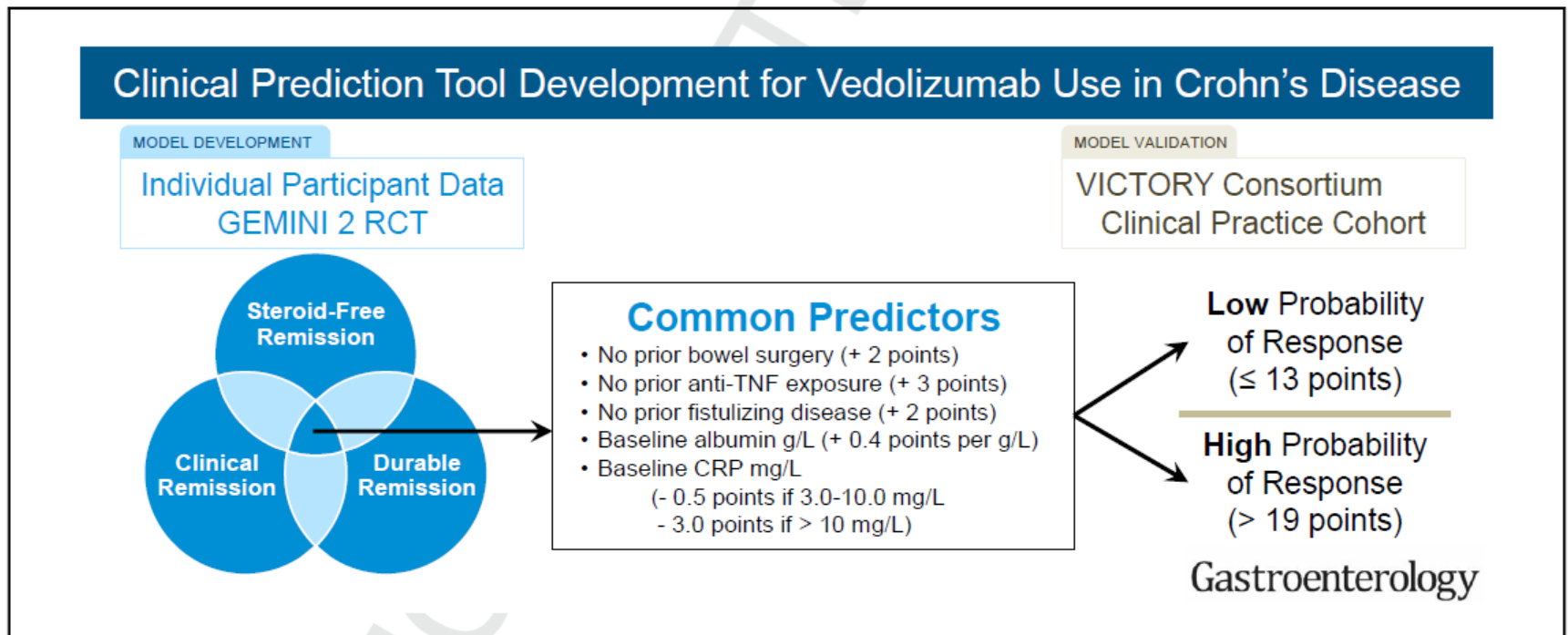
- Comparison of active TB cases across infliximab, golimumab and ustekinumab development programs



Έξυπνη Χρήση Vedolizumab σε Νόσο του Crohn

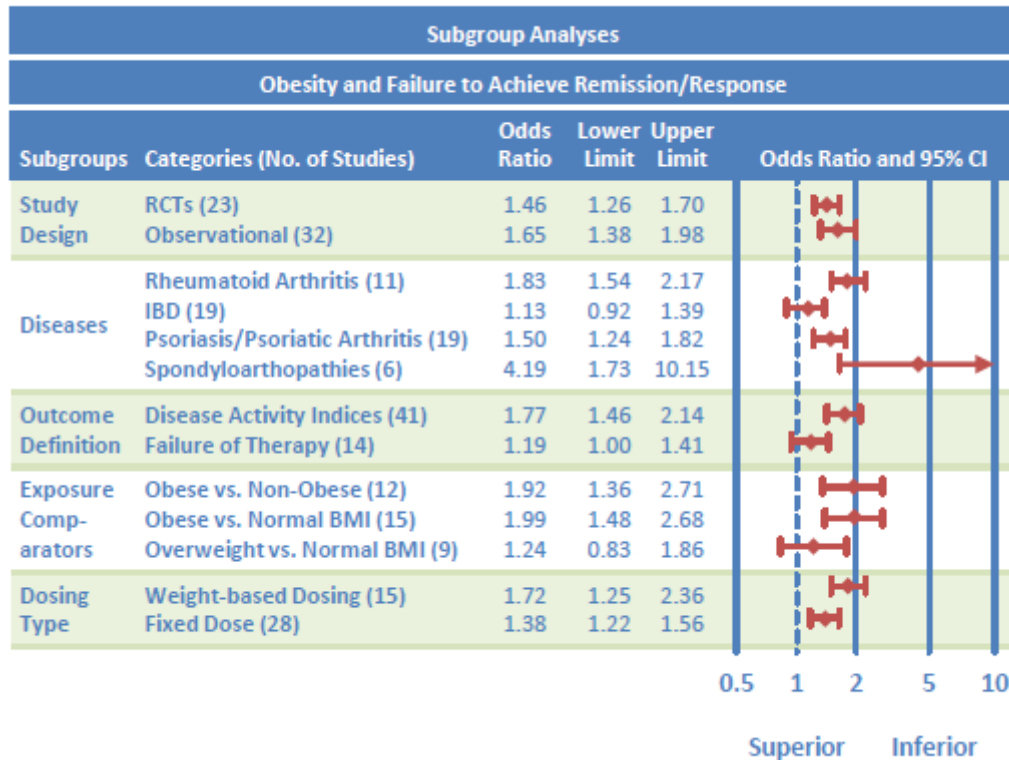


CD: Vedolizumab Precision Tool



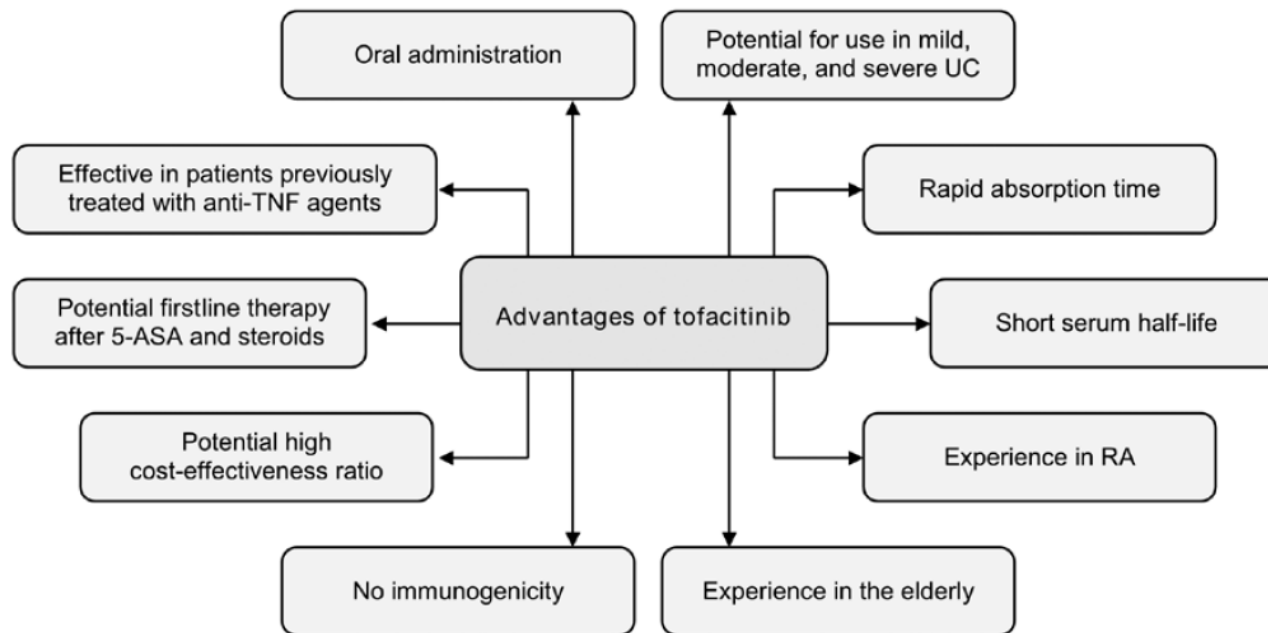
BMI Και Ανταπόκριση σε Βιολογική Θεραπεία

54 cohorts, 19,372 patients



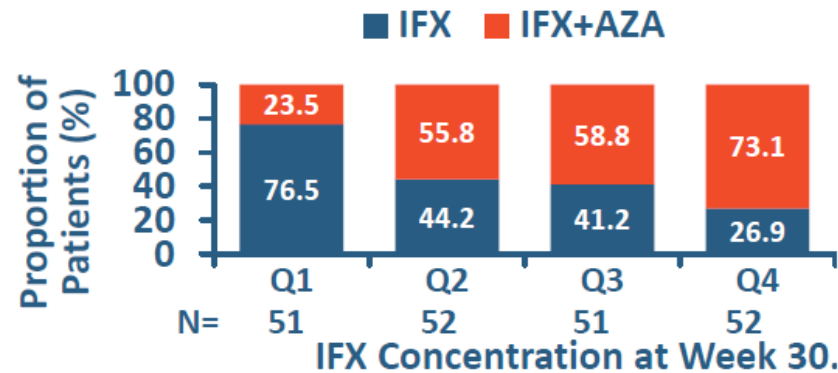
- Σε όλες τις ρευματοπάθειες κακός προβλεπτικός δείκτης απάντησης σε anti-TNF
- 1 Kg/m² αύξηση του BMI, 6,5% υψηλότερη πιθανότητα αποτυχίας anti-TNF
- IBD;

Tofacitinib και Ελκώδης Κολίτιδα

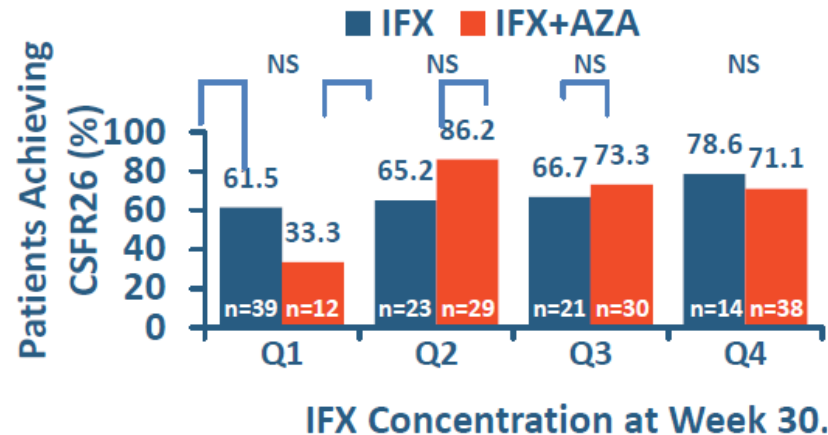


**Ανοσοκαταστολή, Έρπητας Ζωστήρας;
Υπερλιπιδαιμία;
Κύηση;**

SONIC: Infliximab combo vs mono: τα επίπεδα φαρμάκου κάνουν τη διαφορά -TDM



Q1: <0.84 µg/mL; Q2: 0.84 µg/mL to <2.36 µg/mL; Q3: 2.36 µg/mL to <5.02 µg/mL; Q4: ≥5.02 µg/mL



Βιομοειδή-Biosimilars



...Biosimilar infliximab and biosimilar adalimumab are effective treatments for patients with moderate-to-severe Crohn's disease and can be used for de novo induction and maintenance therapy.

ACG Guidelines 2018

Εξατομικευμένη Θεραπευτική Προσέγγιση

✓ **Personalized Medicine**

...is a medical procedure that separates patients into different groups with medical decisions, practices, interventions and /or products being tailored to the individual patient based on their predicted response or risk of disease

Academy of Medical Science

✓ **Precision Medicine**

...a form of medicine that uses information about the patients genes, proteins and environment to prevent, diagnose and treat disease

National Cancer Institute

National research Council

IBD: Personalized Medicine

Personalized medicine: Dream or reality?



Clinical



Serologic



Pharmacogenetics
TDM
Pharmacokinetics



Algorithms,
Web-based
Monitoring
devices



Prediction
of response



Microbiome
Metabolome
Diet
Functional studies



Προγνωστικοί δείκτες ανταπόκρισης σε biologics

- όχι vedolizumab: σε σοβαρή νόσο (κλινικά, ↑δείκτες φλεγμονής)
- ναι ustekinumab: L3 εντόπιση, χωρίς χειρουργείο, χωρίς επιπλοκή

(A)

Predictors of response in Crohn's disease	Anti-TNF alpha	Vedolizumab	Ustekinumab
Patient-related factors			
Young age at initiation	Positive predictor	Insufficient data or controversy	Insufficient data or controversy
Smoking	Negative predictor	Negative predictor	Not examined
High BMI	Negative predictor	Insufficient data or controversy	Not examined
Disease-related factors			
Shorter duration of disease	Positive predictor	Insufficient data or controversy	Insufficient data or controversy
Severe disease activity at induction	Negative predictor	Negative predictor	Negative predictor
Complicated phenotype (stricturing, penetrating)	Negative predictor	Negative predictor	Negative predictor
History of intestinal resection	Negative predictor	Not examined	Not examined
Ileocolonic disease	Positive predictor	Positive predictor	Positive predictor
Elevated inflammatory biomarkers	Positive predictor	Negative predictor	Insufficient data or controversy
No recent hospitalisation (12 months)	Not examined	Positive predictor	Not examined
Treatment-related factors			
Early response	Positive predictor	Positive predictor	Positive predictor
Mucosal healing	Positive predictor	Not examined	Not examined
Low trough level of biologic	Negative predictor	Negative predictor	Negative predictor
Anti-drug antibodies	Negative predictor	Insufficient data or controversy	Insufficient data or controversy
No prior anti-TNF exposure	Positive predictor	Positive predictor	Not examined
Concomitant steroid use	Not examined	Negative predictor	Not examined
Concomitant immunomodulator use	Positive predictor	Insufficient data or controversy	Positive predictor
Others			
Genetic: Fas-ligand-843 TT, caspase-9 93 CC/CT	Negative predictor	Not examined	Not examined
Microbiome: higher alpha diversity	Not examined	Positive predictor	Not examined

(B)

Predictors of response in ulcerative colitis	Anti-TNF alpha	Vedolizumab
Patient-related factors		
Young age	Positive predictor	Not examined
High BMI	Negative predictor	Insufficient data or controversy
Disease-related factors		
Severe disease activity at induction	Negative predictor	Negative predictor
Disease extent	Negative predictor	Not examined
Elevated inflammatory biomarkers	Insufficient data or controversy	Negative predictor
High hemoglobin at baseline	Positive predictor	Not examined
Low serum albumin	Negative predictor	Insufficient data or controversy
pANCA +	Negative predictor	Not examined
Treatment-related factors		
Early response	Positive predictor	Positive predictor
Mucosal healing	Positive predictor	Not examined
Low trough level of biologic	Negative predictor	Negative predictor
Anti-drug antibodies	Negative predictor	Insufficient data or controversy
No prior anti-TNF exposure	Positive predictor	Positive predictor
Concomitant steroid use	Not examined	Negative predictor
Concomitant immunomodulator use	Positive predictor	Not examined
Others		
Genetic: high expression oncostatin M, TNF receptor 1 36G	Negative predictor	Not examined

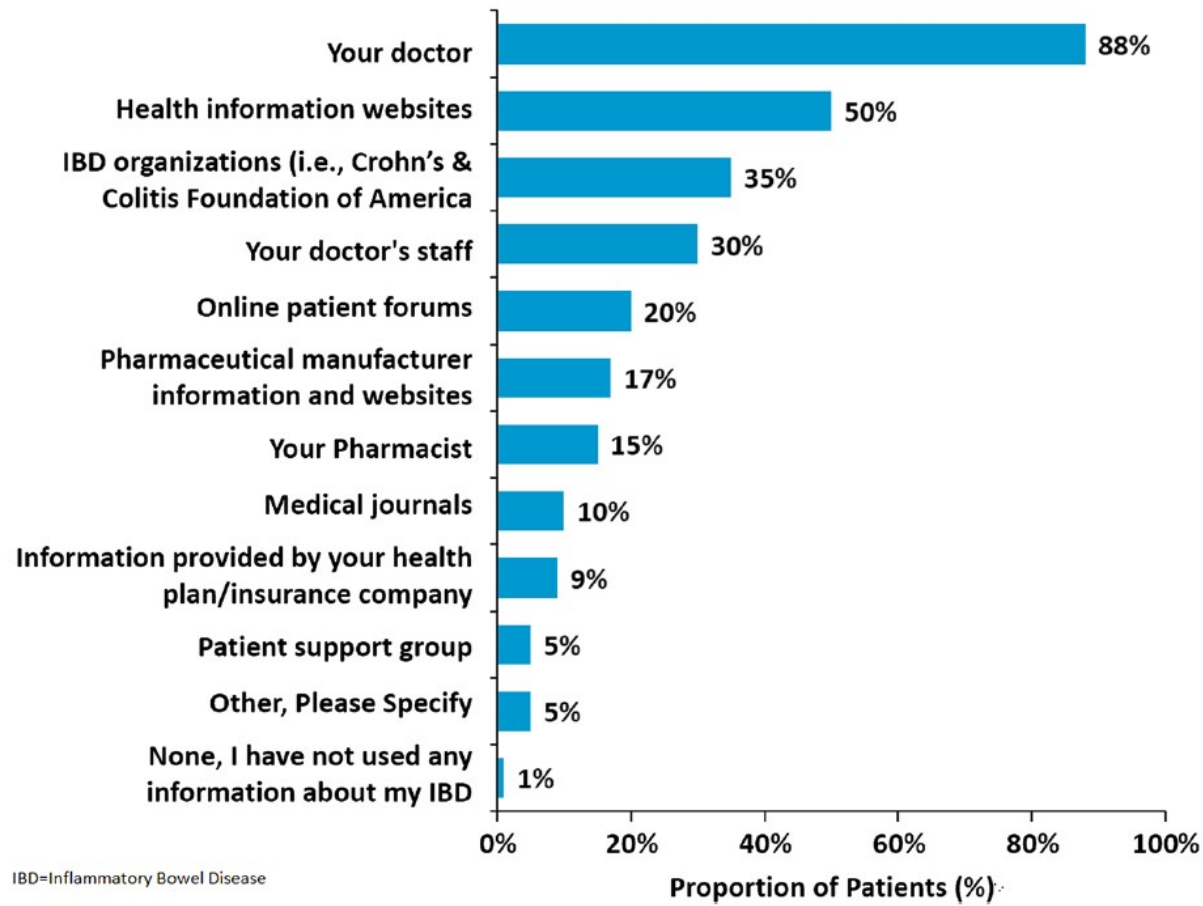
Positive predictor

Insufficient data or controversy

Negative predictor

Not examined

Shared decision Making: εφικτό;



Προτίμηση Ασθενή; Μη προβλέψιμη! (δημογραφικά, χαρακτηριστικά της πάθησης)

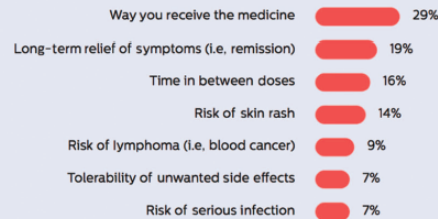


ABOUT THIS REPORT

This is your IBD&me Personalized Report. It shows what was most important to you as you were deciding among the different biologic medicines. You can [print out the Report and bring it with you to the doctor](#), or you can [send it in an email to your doctor](#).

Below, you will see your "Importance Scores" for the seven biologic characteristics from the IBD&me Decision Tree. The higher the score, the more important the characteristic is to you when choosing among medicines. If you want to learn more about Importance Scores or how you can use this report, please visit the [FAQs](#).

MY IMPORTANCE SCORES



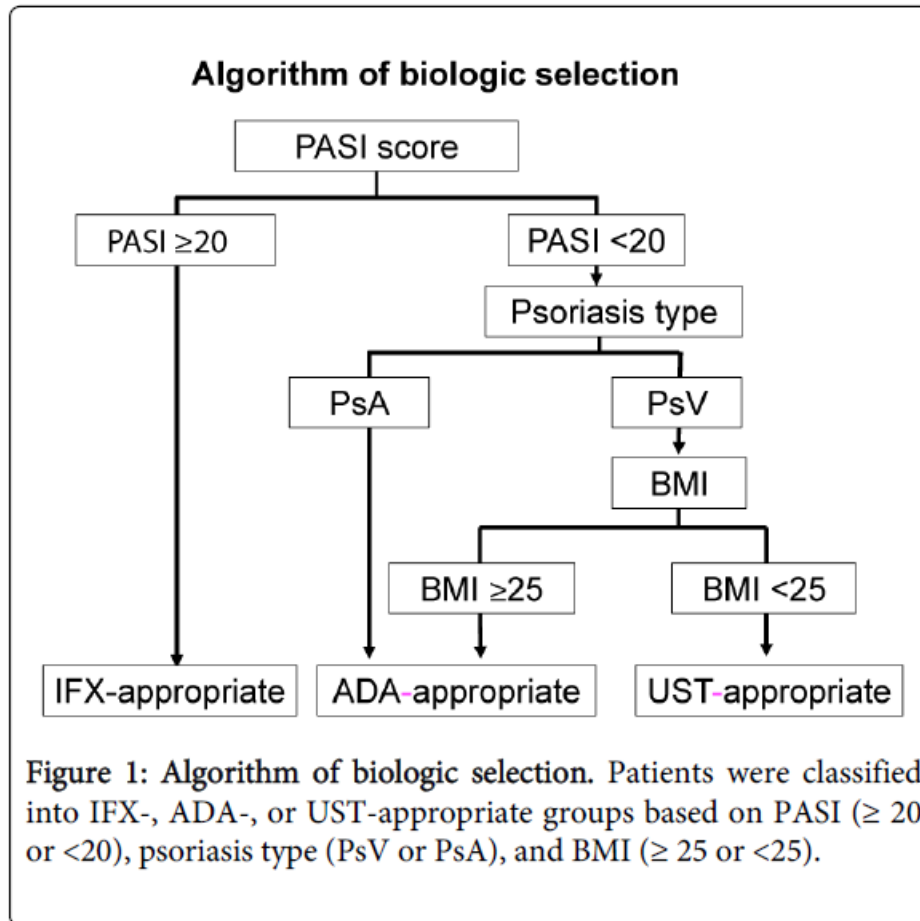
WHAT DOES THIS MEAN?

Based on your responses, these were the [top 3 most important factors](#) for you as you were choosing among the different biologic medicines. It also seems that you prefer to receive the medicine [given through an IV into the vein in your home](#) and want it [given every 8 weeks](#).



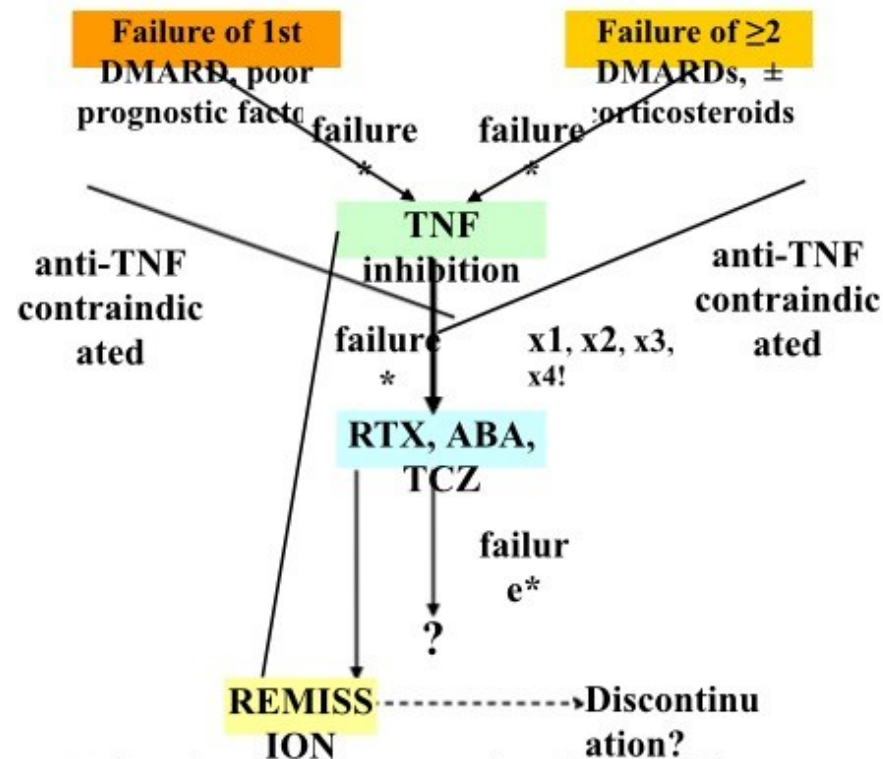
- Μηχανισμός δράσης;
- Τρόπος χορήγησης;
- Αποτελεσματικότητα;
- ταχύτητα δράσης
- διάρκεια καλού αποτελέσματος
- Ασφάλεια;
- λοιμώξεις
- λέμφωμα
- εξάνθημα

Επιλογή Βιολογικών στην Δερματολογία Ψωρίαση



Επιλογή Βιολογικών στην Ρευματολογία

Ρευματοειδής Αρθρίτιδα



Failure*: primary or secondary loss of efficacy, intolerance. Even moderate response!
(After optimizing DMARD dose and/or trying combination of DMARDs).

Επιλογή Βιολογικού Παράγοντα 2018

Αποτελεσματικότητα

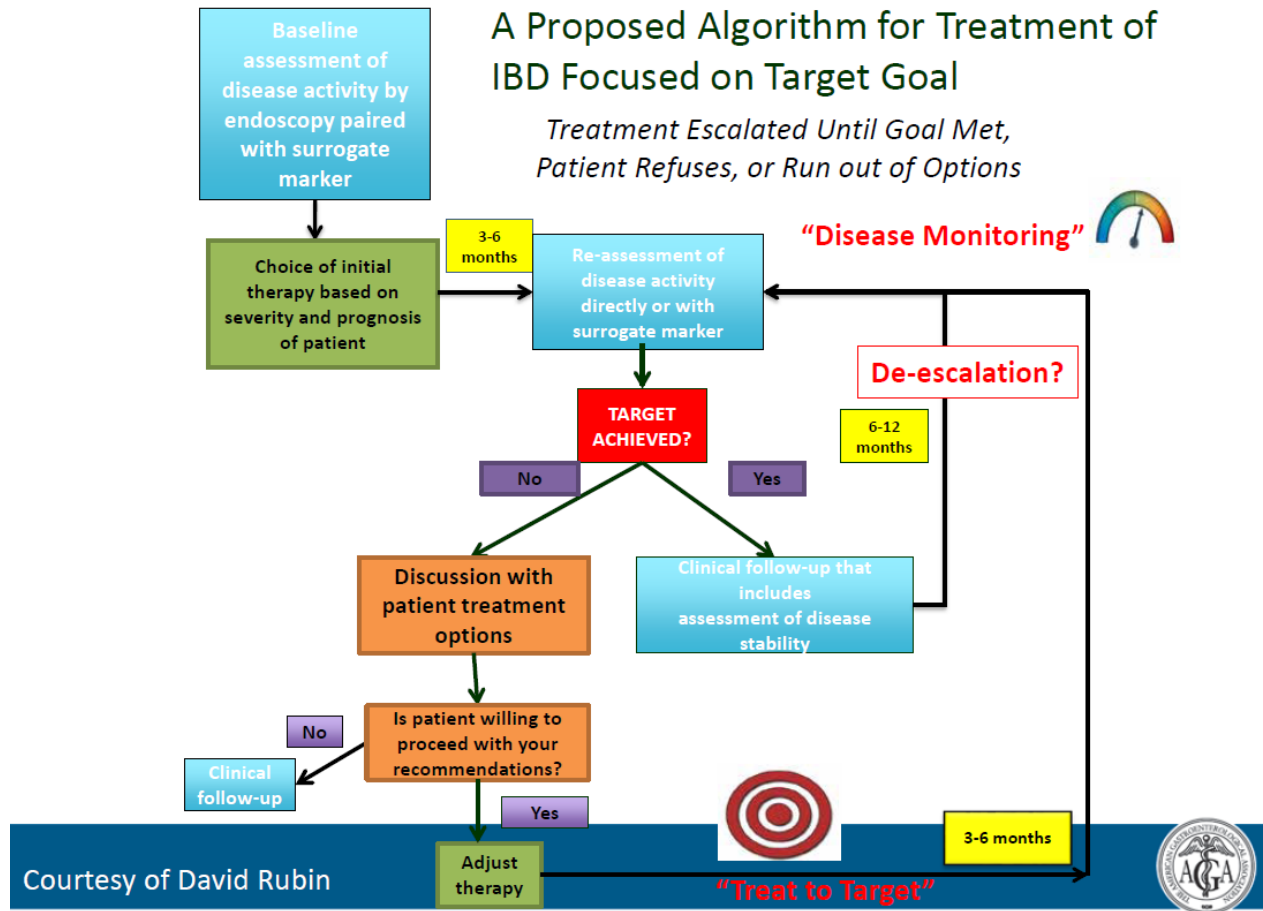
Δραστηριότητα Νόσου
Έκταση και Εντόπιση
Εξωεντερικές Εκδηλώσεις
Συρίγγια
Οξεία Βαριά Κολίτιδα
Σωματικό βάρος

Ασφάλεια

Ηλικία (<18, 18-65, >65)
Λοιμώξεις
Λέμφωμα (καρκίνος;)
Απομυελινωτική Νόσος
Καρδιακή Ανεπάρκεια
Κύηση

Προτίμηση ασθενή
Οδός Χορήγησης
Διαθεσιμότητα
Κόστος

Ανεξάρτητα από επιλογή, T2T



Ευχαριστώ Πολύ



ΕΛΛΗΝΙΚΗ ΓΑΣΤΡΕΝΤΕΡΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
ΤΜΗΜΑ ΒΟΡΕΙΟΥ ΕΛΛΑΔΟΣ "ΜΑΚΕΔΟΝΙΑ"

Επιστημονική
Εκπαιδευτική
Διημερίδα

5-6
ΟΚΤΩΒΡΙΟΥ
2018

Ολυμπιακό
Μουσείο
Θεσσαλονίκης

