# Τι νεότερο στις Σπονδυλοαρθρίτιδες

**ΠΕΛΑΓΙΑ ΚΑΤΣΙΜΠΡΗ**

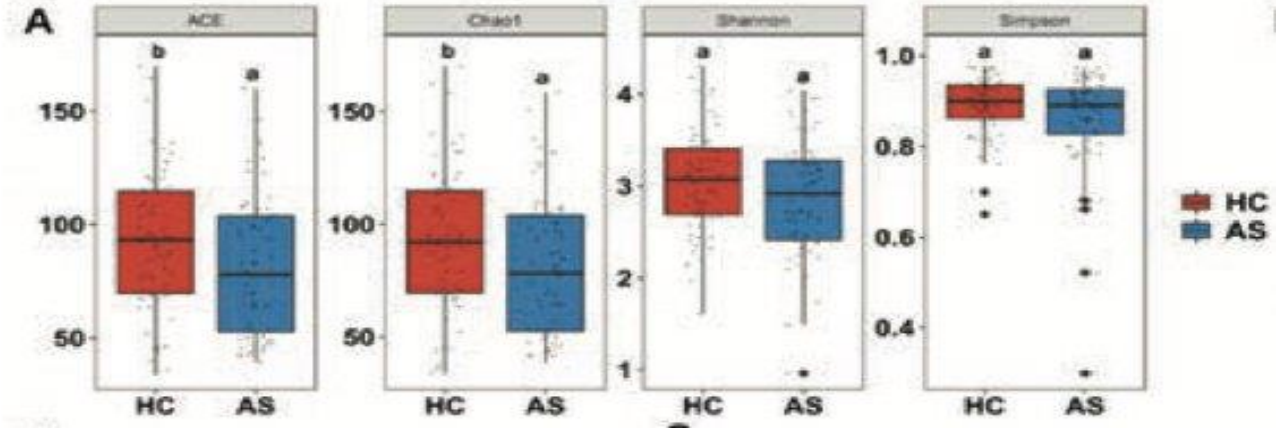
ΕΠΙΜΕΛΗΤΡΙΑ Α’ ΕΣΥ

ΡΕΥΜΑΤΟΛΟΓΟΣ

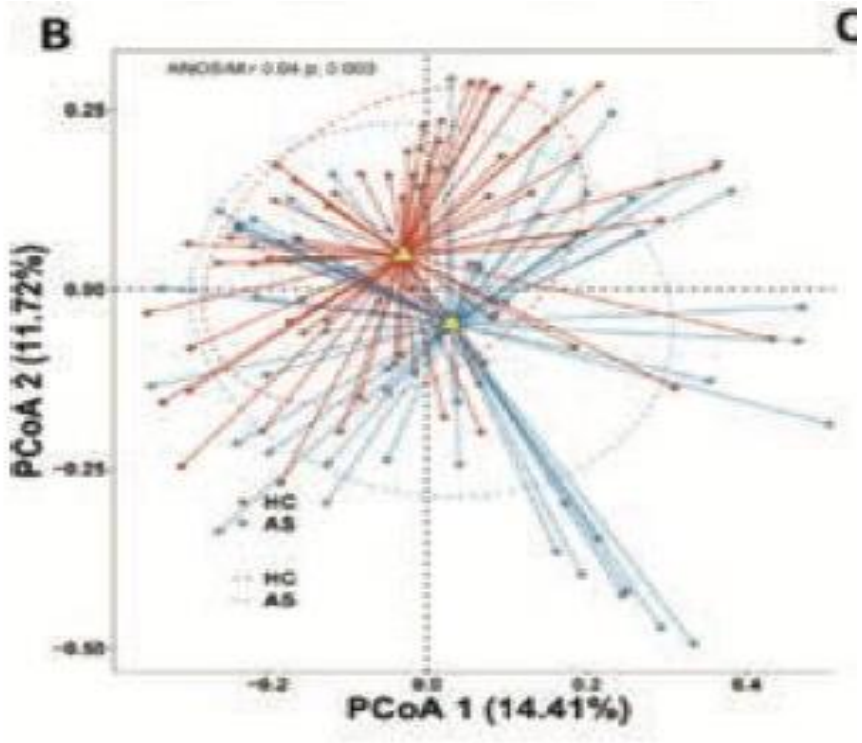
Δ’ ΠΑΘΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ

ΠΑΝ/ΚΟ ΓΕΝ. ΝΟΣ. ΑΤΤΙΚΟΝ

# SpA Pathogenesis: Gut microbiota in AS patients and Healthy Controls




(A) Alpha-diversity assessed by richness (Chao 1, ACE) and diversity (Shannon, Simpson) , Median estimates compared across cohorts

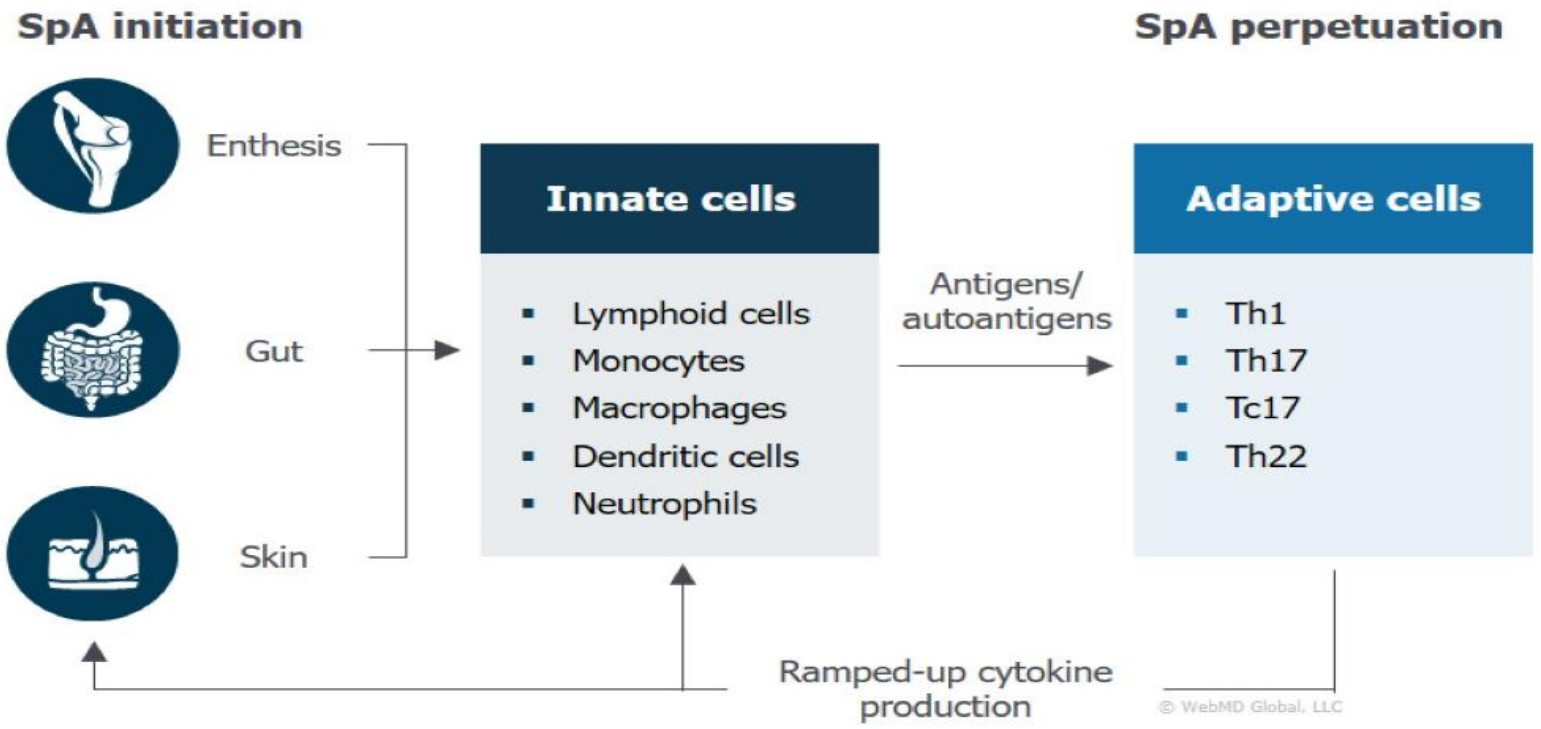



PCoA plot based on the Bray Curtis distance of gut microbiota samples from AS patients vs HC group (p=0.003, ANOSIM).



EULAR2022 ABST#POS0330

# Malfunction of Innate and Adaptive Immune Responses in SpA Pathogenesis

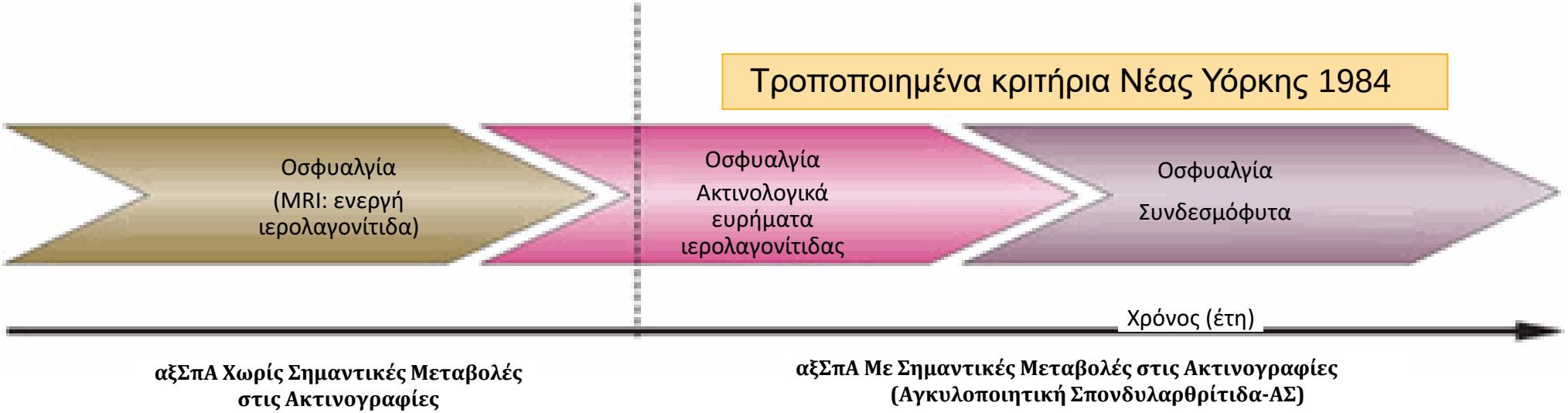



1. Microbial-injured tissue activates aberrant immune response(skin or gut)
2. Activated immune cells arrive at and interact with target tissues triggering inflammation and damage
3. IL-23 is released at entheseal sites or the gut and acts on Th17 cells releasing IL-17A and IL-17F ( which play a major role in axSpA pathogenesis

AxSpA, axial spondyloarthritis; IL, interleukin; SpA, spondyloarthritis.
a. Gill T, et al. Front Immunol. 2021;11:586494; b. Sharif K, et al. Rheumatology. 2020;59:iv67-iv78; c. Veale DJ, et al. Rheumatology. 2019;58:197-205.

# Εξέλιξη της Νόσου με Σημαντικές Μεταβολές στις Ακτινογραφίες

- Η αξονική σπονδυλαρθρίτιδα περιλαμβάνει[1,2]
  - Την αγκυλοποιητική σπονδυλαρθρίτιδα (ΑΣ) ***και***
  - Την αξΣπΑ χωρίς ακτινολογικά ευρήματα στις ακτινογραφίες .

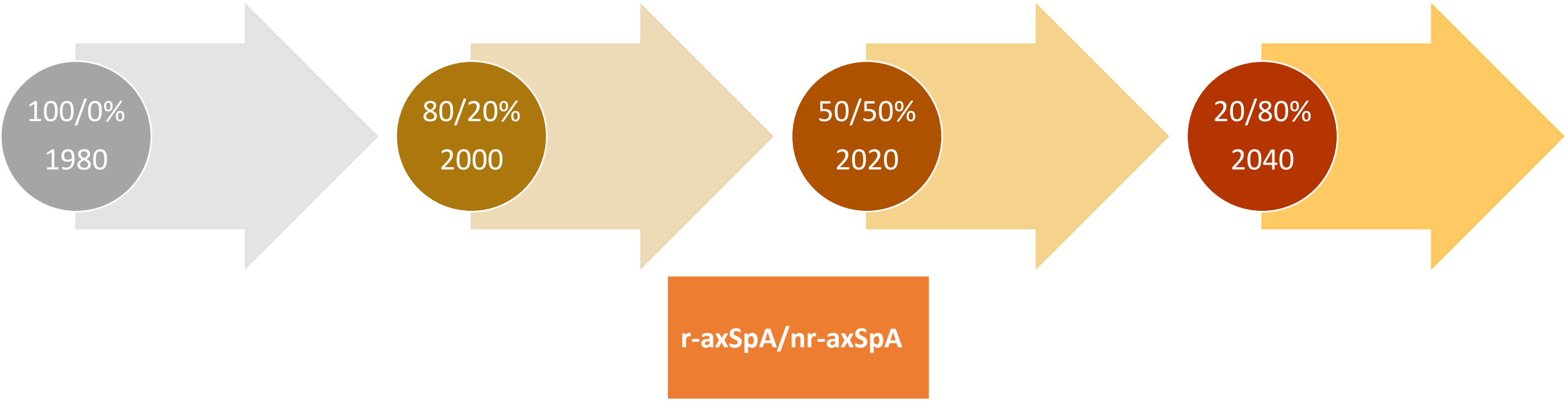



- Δεν εξελίσσονται όλοι οι ασθενείς από αξΣπΑ χωρίς ακτινολογικά ευρήματα σε αγκυλοποιητική σπονδυλαρθρίτιδα[2]
- Τα ποσοστά εξέλιξης από αξΣπΑ χωρίς ακτινολογικά ευρήματα σε ΑΣ παραμένουν ασαφή[2,3]

αξΣπΑ, αξονική σπονδυλαρθρίτιδα, MRI, μαγνητική τομογραφία.

1. Rudwaleit M et al. *Ann Rheum Dis.* 2009;68:777-783;
2. Rudwaleit M et al. *Nat Rev Rheumatol.* 2012;8:262-268;
3. Poddubnyy D et al. *Ann Rheum Dis.* 2011;70:1369-1374.

# Κατανομή των υποτύπων ax-SpA με την πάροδο του χρόνου




Κατανομή των υποτύπων της AxSpA με την πάροδο του χρόνου.
Εκτίμηση της αναλογίας επιπολασμού μεταξύ r-axSpA και nr-axSpA, για κάθε χρονική περίοδο κατά τη στιγμή της διάγνωσης.

Adapted from Benavent *et al*. Clin Rheumatol. 2021 Feb;40(2):501–512
Ann.Rheum.Dis 2021;80:1511-21

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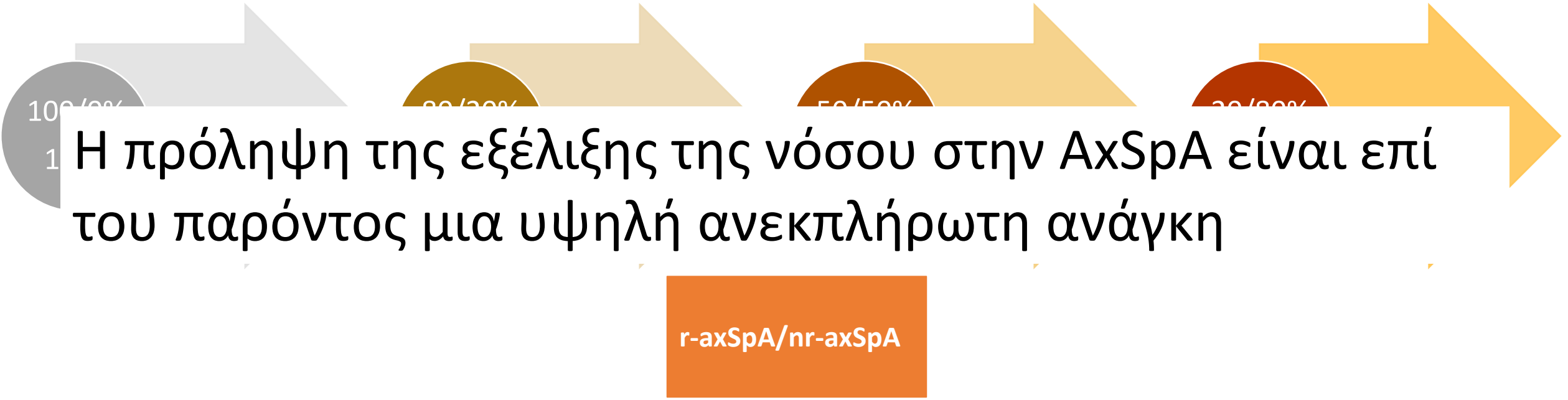



Η πρόληψη της εξέλιξης της νόσου στην AxSpA είναι επί του παρόντος μια υψηλή ανεκπλήρωτη ανάγκη

Κατανομή των υποτύπων της AxSpA με την πάροδο του χρόνου.
Εκτίμηση της αναλογίας επιπολασμού μεταξύ r-axSpA και nr-axSpA, για κάθε χρονική περίοδο κατά τη στιγμή της διάγνωσης.

Adapted from Benavent *et al*. Clin Rheumatol. 2021 Feb;40(2):501–512
Ann.Rheum.Dis 2021;80:1511-21

# EULAR and ACR TREATMENT GOALS for axSpA

## ASAS-EULAR[1]

The primary goal of treating the patient with axSpA is to maximize HRQoL through:

- Control of symptoms and inflammation
- Prevention of progressive structural damage
- Preservation/normalization of function and social participation

## ACR/SPARTAN/SAA[2]

The goals of treatment of r-axSpA and nr-axSpA are to:

- Alleviate symptoms
- Improve functioning
- Maintain ability to work
- Decrease disease complications
- Prevent progressive structural damage

Treatment of patients with axSpA should be individualized based on current signs and symptoms of disease (axial, peripheral, extra-musculoskeletal manifestations) and patient characteristics, which include comorbidities and psychosocial factors[1]

# EULAR/ASAS 2022 updated AxSpA Treatment Guidelines

## Overarching Principles - Unchanged since 2016

- **axSpA is a potentially severe disease with diverse manifestations, usually requiring multidisciplinary management coordinated by the rheumatologist.**
- The primary goal of treating the patient with axSpA is to maximize health-related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, preservation/normalization of function, and social participation.
- **The optimal management of patients with axSpA requires a combination of non-pharmacological and pharmacological treatment modalities**
- Treatment of axSpA should aim at the best care and must be based on a shared decision between the patient and the rheumatologist
- **axSpA incurs high individual, medical and societal costs, all of which should be considered in its management by the treating rheumatologist**



S. Ramiro EULAR 2022

# EULAR/ASAS 2022 updated AxSpA Guidelines Recommendations

Recommendations increased from 13 to15

**Two previous recommendations** dealing with drug therapy **revised significantly**

**Recommendation 9**: For patients with persistently high disease activity despite conventional therapy, a TNF inhibitor**, <u>including</u>** the pegylated humanized antigen-binding fragment certolizumab pegol, an IL-17i, or JAKi, should be considered. *Changed from <<current practice is to start with TNFi therapy>>*

**Previous recommendation 10 NOW recommendation 12**. Revised to << Following 1st biologic or tsDMARD failure, switching to another bDMARD (TNFi or IL-17i) or JAKi should be considered.>> from <<If TNFi therapy fails, switching to another TNFi* or IL-17i** therapy should be considered>>



S. Ramiro EULAR 2022

# EULAR/ASAS 2022 updated AxSpA Guidelines Recommendations

**Two new recommendations** added

**New recommendation 10: If there is a history of recurrent uveitis or active IBD, preference should be given to a monoclonal abTNFi. For patients with significant psoriasis, an IL-17Ai may be preferred.**

**New recommendation 11:Absence of response to treatment should trigger re-evaluation of the diagnosis and consideration of the presence of comorbidities**



S. Ramiro EULAR 2022

# ACR-EULAR ομοιότητες και διαφορές στις συστάσεις θεραπείας axSpA

- Μια κύρια διαφορά είναι η μεθοδολογία που χρησιμοποιείται για να φτάσουμε στη σύσταση.
- Η μεθοδολογία ACR χρησιμοποιεί τη μέθοδο'PICO' — population, intervention, control, και outcomes. Όταν υπάρχουν ισχυρές αποδείξεις η σύσταση έχει βαρύτητα αλλά όταν απουσιάζουν τότε οι συστάσεις είναι υπό όρους.
- Οι συστάσεις ASAS/EULAR βασίζονται σε ευρύτερα επίπεδα αποδεικτικών στοιχείων και σε συναίνεση.
- Οι συστάσεις ASAS/EULAR έχουν λάβει υπόψη νεότερα φάρμακα που έχουν εγκριθεί από το 2019.
- Διαφορές σε ζητήματα όπως η T2T, και η επανεξέταση της διάγνωσης όταν η θεραπεία αποτύχει.
- Συμφωνία για τη χρήση ΜΣΑΦ, την άσκηση, την έναρξη bDMARD σε ενεργό νόσο παρά τη συμβατική θεραπεία και την αποφυγή csDMARDs στην αξονική νόσο (High level of evidence).

# Συστάσεις για τη θεραπεία της αξΣπΑ

**1ο Βήμα**

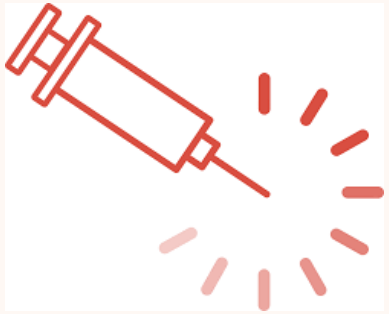
- ΜΣΑΦ

**2ο Βήμα**

- bDMARD (TNFI ή IL-17i) ή tsDMARD (JAKi)

**Εκπαίδευση**
**Άσκηση και φυσιοθεραπεία**
**Παυσίπονα**
**Χειρουργείο**

# Νέες θεραπείες στην αξ ΣπΑ



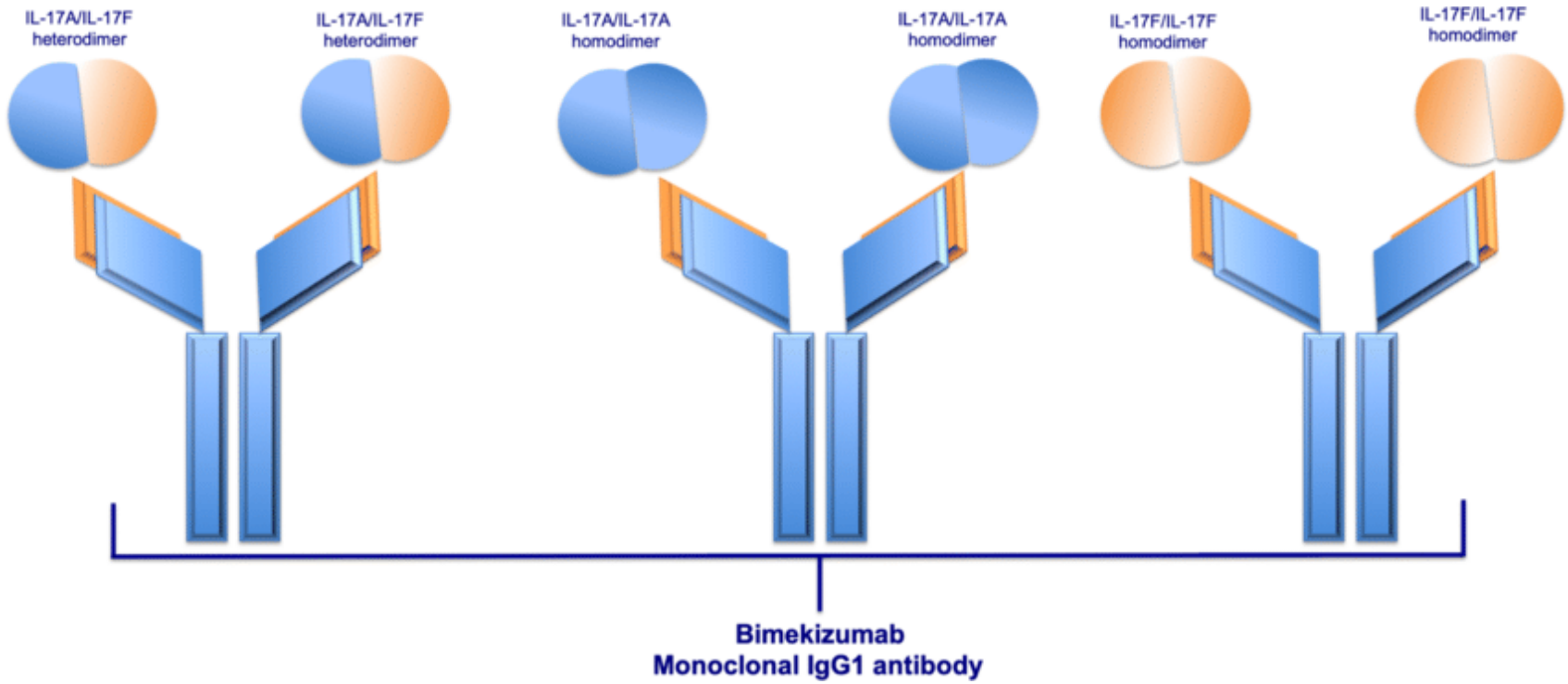
## IL-17 inhibitors

Bimekizumab (r and nr axSpA)

## JAK inhibitors

Upadacitinib (nr axSpA)

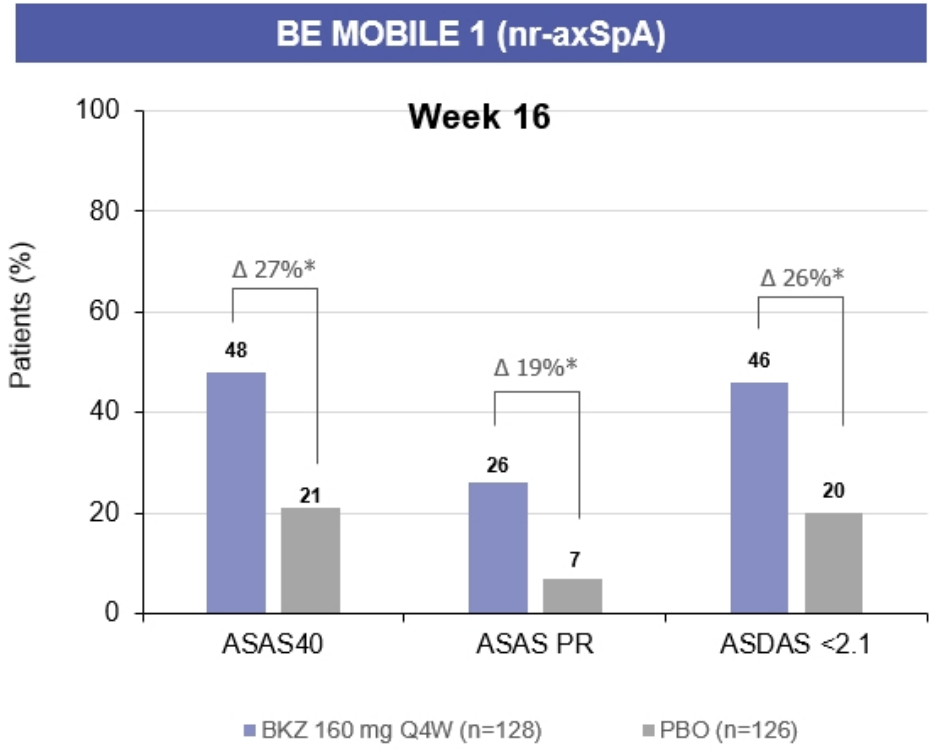
# IL-17i
## Bimekizumab

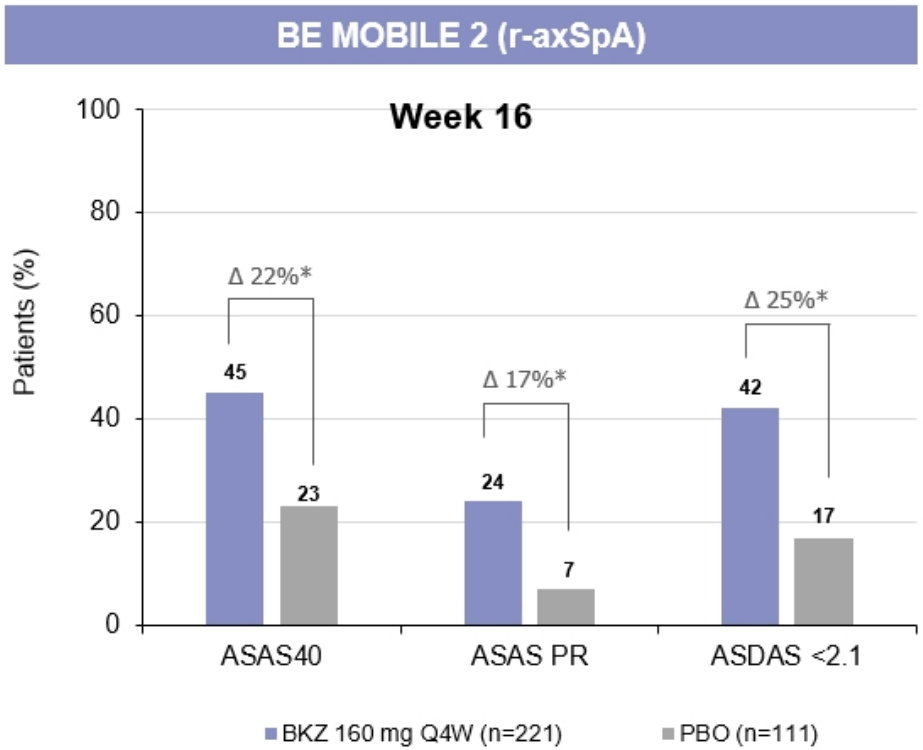



**Bimekizumab (BKZ), is a humanized monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL17A**

Blauvelt, Andrew & Chiricozzi, Andrea & Ehst, Benjamin. (2020). Bimekizumab. Current Dermatology Reports. 9. 1-7. 10.1007/s13671-020-00286-2.

# Bimekizumab: Αποτελεσματικότητα στην αξΣπΑ




the Phase 3 BE MOBILE 1 study in non-radiographic axSpA and the Phase 3 BE MOBILE 2 study in ankylosing spondylitis met the primary and all ranked secondary endpoints in both studies showing consistent improvements versus placebo in signs and symptoms across the full spectrum of axSpA, including non-radiographic axSpA and ankylosing spondylitis.

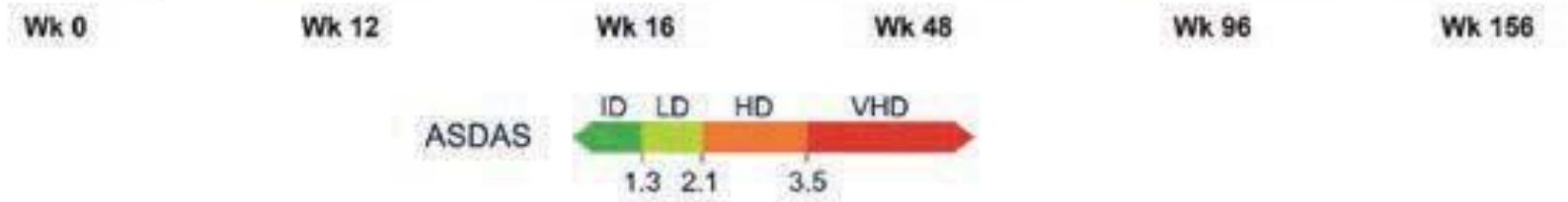
*p<0.001. ASAS: Assessment of Spondyloarthritis International Society; ASAS40: Assessment in SpondyloArthritis international Society 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BKZ: bimekizumab; IL: interleukin; MI: major improvement; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; PR: partial remission; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis

1. Deodhar A, et al. Presented at EULAR 2022. Abstract number 2416;
2. van der Heijde D, et al. Presented at EULAR 2022. Abstract number 2441

# Bimekizumab: long term results


**Safety**:

In all studies the safety profile of bimekizumab was consistent with other studies with IL-17i with no new observed safety signals. The most frequently reported AE were upper respiratory tract infections (14.5 percent) (most frequently nasopharyngitis) and oral candidiasis (7.3 percent).



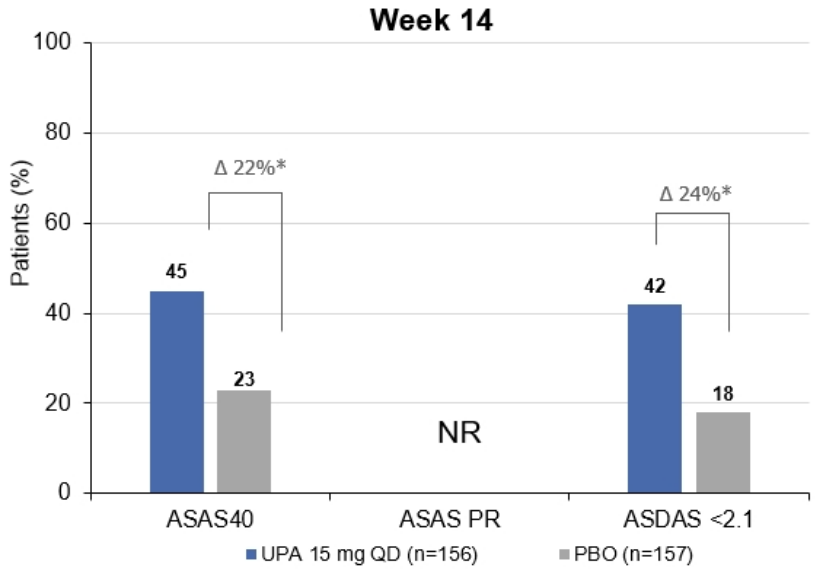

The 3 year results from the open-label extension of the phase 2b BE AGILE study show maintenance of the disease control in those that had initially responded at week 12.



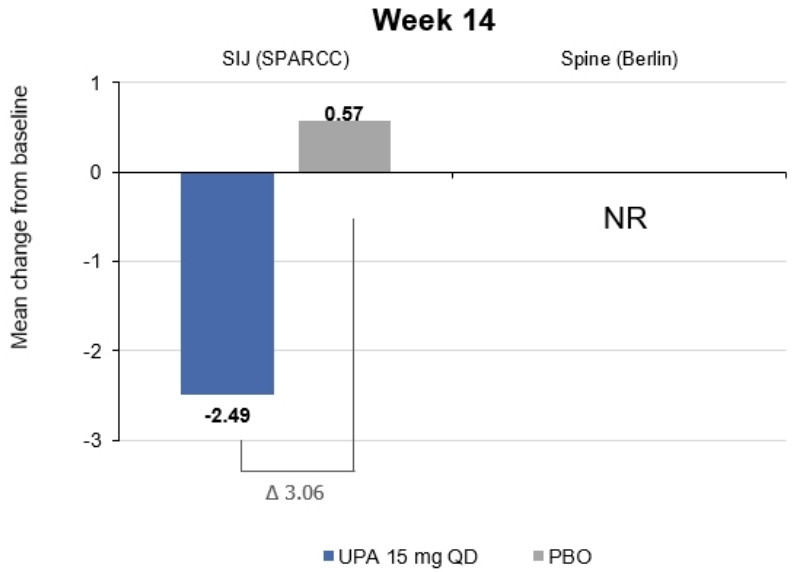
V. Navarro-Compán et al.Eular 2022.ABSTRACT NO 2138

# Upadacitinib in nr-axSpA: Select-AXIS 2

**Efficacy**




**MRI scores**




**Prior bDMARD-exposure was permitted**

The SELECT-AXIS 2 nr- ax SpA: multicentre, randomised, double-blind, placebo-controlled, phase 3 trial at 113 sites across 23 countries.

Objective signs of inflammation based on MRI or elevated C-reactive protein and NSAID-IR.

The primary endpoint was the ASAS40 response at week 14 which was met.

UPA 15 mg QD demonstrated significantly greater improvements in disease activity, pain, function, quality of life, and MRI-detected SI joint inflamma- tion than PBO after 14 wks of treatment in pts with active nr-axSpA. The safety profile of UPA was consistent with what has been observed with other inflamma- tory musculoskeletal diseases,3–5 and no new risks were identified.

*p<0.0001
ASAS40: Assessment of SpondyloArthritis international Society 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; LDA, low disease activity; PBO: placebo; r-axSpA: radiographic axial spondyloarthritis; NR, not reported; nr-axSpA: non-radiographic axial spondyloarthritis; QD: once a day; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada; UPA: upadacitinib



10.1136/annrheumdis-2022-eular.2534

# Upadacitinib in nr-axSpA: Select-AXIS 2 safety data

Safety data were consistent with other studies in all indications.
No new risks identified. The proportion of pts who experienced a TEAE was similar between treatment groups

| | UPA | PBO |
|---|---|---|
| ALL TEAE % | 48 | 46 |
| SERIOUS TEAE (discont) (%) | 4 (2.6) | 2(1.3) |
| SERIOUS INFECTION | 2 (1.3) | 1 (0.6) |
| HERPES ZOSTER | 2 (1.3) | 1 (0.6) |
| UVEITIS | 1(0.6%) | 0 |
| MALIGNANCY OTHER THAN NON-MELANOMA SKIN CANCER | 0 | 1 (Basal cell carcinoma) |
| CV, VTE, IBD | 0 | 0 |
| DEATH | 0 | 0 |

JAKi: Janus kinase inhibitor; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; QD: once a day; UPA: upadacitinib



doi.org/10.1016/S0140-6736(22)01212-0

# ASAS quality standards to improve the quality of health and care services for patients with axial spondyloarthritis.

| DIAGNOSIS | TREATMENT | MANAGEMENT |
|---|---|---|
| < 3 days | At least every 6 months | < 2 months from diagnosis |
| **QS1. Referral** (suspicion of axSpA) | **QS4. Monitoring** (ASDAS, alt: BASDAI and CRP) | **QS7. Education and self-management** (utilities, treatment options and healthy lifestyle) |
| < 3 weeks | | < 2 working days |
| **QS2. Time to specialist** (rheumatologist and health professionals) | **QS5. Disease control** (treatment escalation, target: remission/LDA) | **QS8. Rapid access** (if flare or drug side effect) |
| < 2 months | | |
| **QS3. Assessment** (history taken, lab, imaging) | **QS6. Non-pharma treatment** (information on regular exercise) | **QS9. Annual review** (clinical symptoms, disease severity, comorbidities) |

# Predicting CV risk score in AxSpA patients

Aim: to establish whether persistently high CRP and high disease activity may be considered predictive factors of CVD in axSpA in 295 patients with axSpA and without personal history of CVD.
High disease activity  defined as ASDAS > 2.1, and BASDAI > 4.
During the follow-up 23 patients had a CV event

**Persistence of increased CRP levels and high disease activity may be considered biomarkers to identify those axSpA patients at higher risk of CVD.**

**Innovative axSpA-specific CV risk score, including these variables, have to be developed.**

**Strong association between CV event and the persistency of increased CRP levels** (HR = 1.03, 95%CI 1.015-1.045, p < 0.001),
**of ASDAS > 2.1** (HR = 1.014, 95%CI 1.000-1.028, p = 0.047),
**and of BASDAI > 4** (HR 1.019, 95%CI 1.006-1.033, p = 0.006) during follow-up, after adjustment for age, sex, and diabetes.



L. Navarini et al.Sci Rep 2022 May 7;12(1):7498.doi: 10.1038/s41598-022-1

# ΣΥΜΠΕΡΑΣΜΑΤΑ

Είχαμε σημαντική πρόοδο στη κατανόηση της παθοφυσιολογίας στις αξΣπΑ.

Την τελευταία δεκαετία έχει σημειωθεί ουσιαστική πρόοδος στη διαχείριση της αξΣπΑ με τη προσθήκη νέων DMARD όπως IL-17i και JAKi.

Με την εμφάνιση νέων θεραπειών, εξελίσσονται επίσης οι θεραπευτικοί αλγόριθμοι.

Η φλεγμονή στις axSpA επιβαρύνει τη νοσηρότητα και τη θνησιμότητα της νόσου.

Χρειαζόμαστε μακροπρόθεσμα δεδομένα από μεγάλες κοόρτες ασθενών για να αξιολογήσουμε εάν μια πιο επιθετική ρύθμιση της φλεγμονής θα αλλάξει τη πορείας της νόσου στις αξΣπΑ.


# ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗ ΠΡΟΣΟΧΗ ΣΑΣ