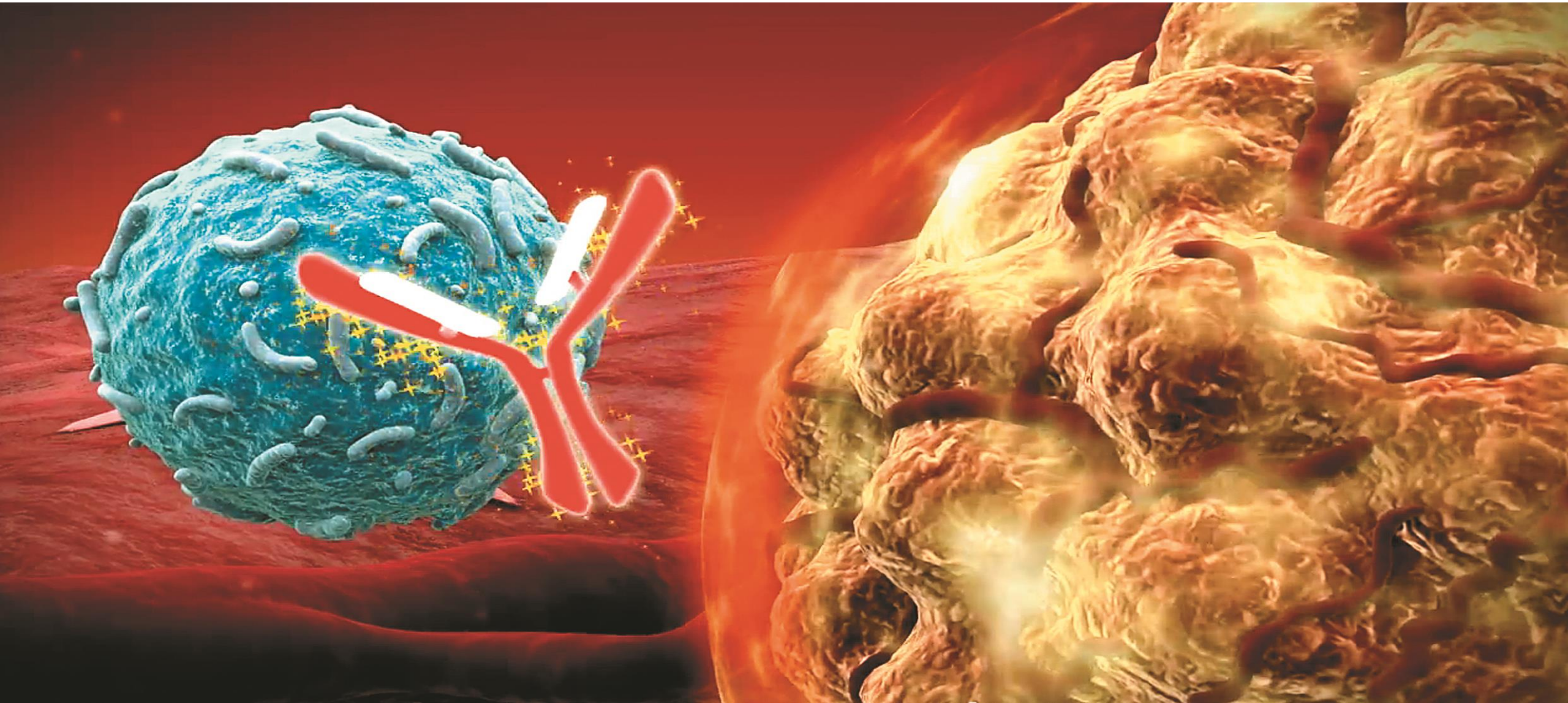
ΑΝΟΣΟΘΕΡΑΠΕΙΑ ΚΑΙ ΡΕΥΜΑΤΟΛΟΓΙΑ



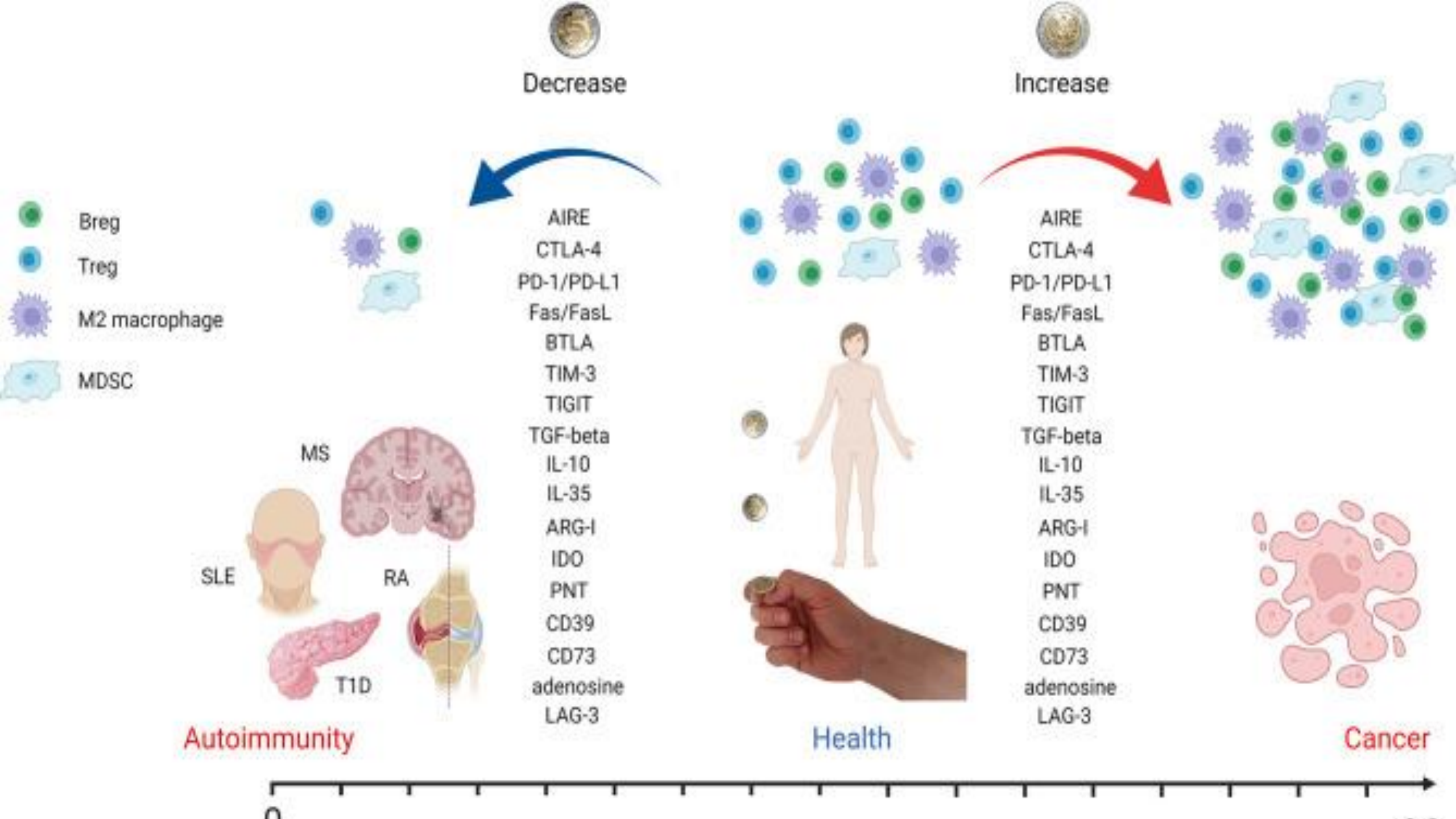
- Δεν έχω καμιά σύγκρουση συμφερόντων.

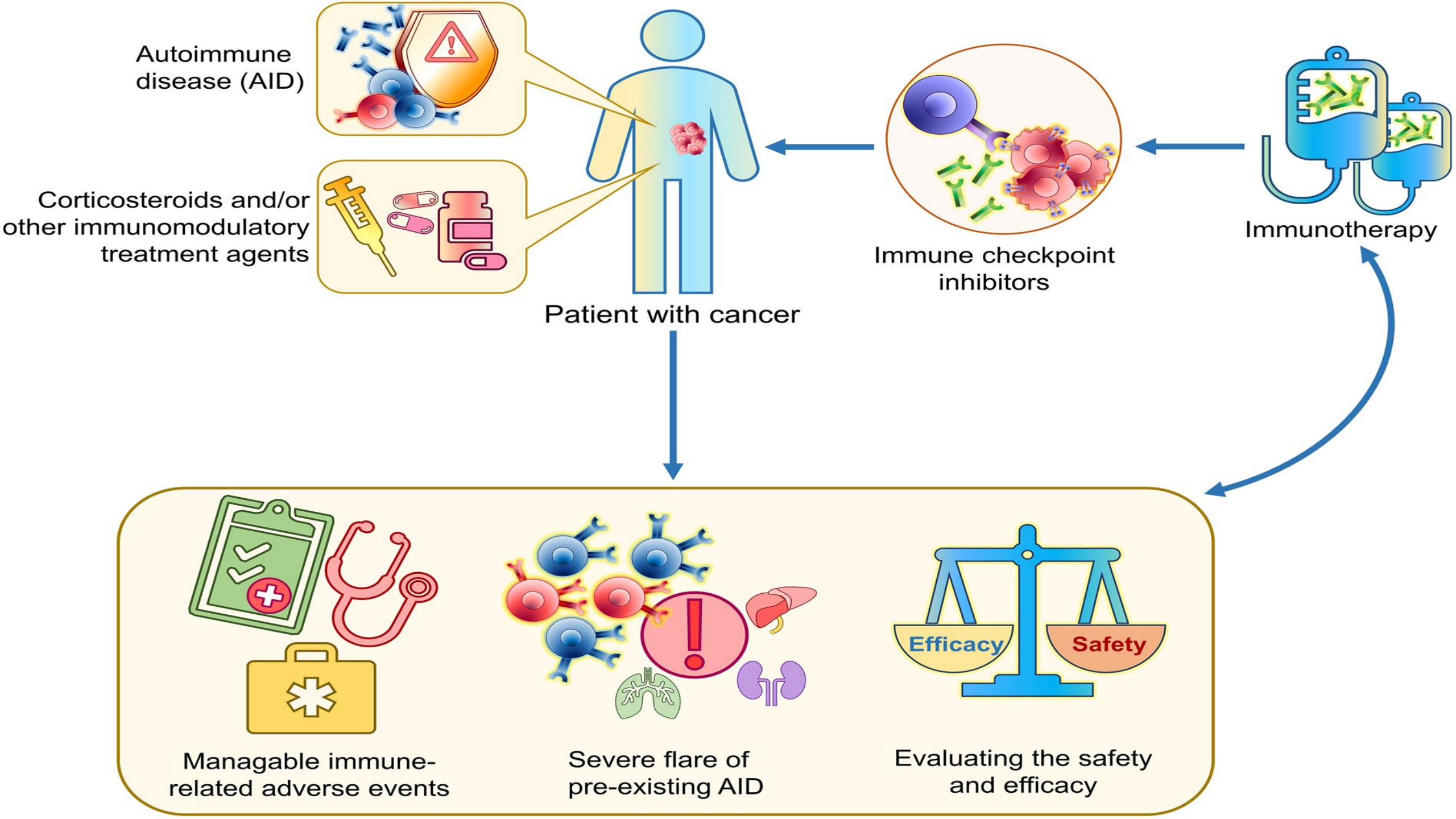
Βιοδείκτες.....

- Η εκφρασή του βιοδείκτη **PDL-1** στα καρκινικά κύτταρα. Όσο μεγαλύτερη έκφραση του δείκτη σε ποσοστό τόσο μεγαλύτερη πιθανότητα για ανταπόκριση.

- **TMB**(tumor mutational burner):Συνολικός αριθμός μεταλλάξεων που υπάρχουν στο γονιδίωμα του όγκου.

- **MSI-H/dMMR**: Υψηλή μικροδορυφορική αστάθεια είναι δείκτης για χορήγηση ανοσοθεραπείας.


Decrease
Increase
Breg
Treg
M2 macrophage
MDSC
AIRE
CTLA-4
PD-1/PD-L1
Fas/FasL
BTLA
TIM-3
TIGIT
TGF-beta
IL-10
IL-35
ARG-I
IDO
PNT
CD39
CD73
adenosine
LAG-3
MS
SLE
RA
T1D
Autoimmunity
Health
Cancer


Autoimmune disease (AID)
Corticosteroids and/or other immunomodulatory treatment agents
Patient with cancer
Immune checkpoint inhibitors
Immunotherapy
Efficacy
Safety
Managable immune-related adverse events
Severe flare of pre-existing AID
Evaluating the safety and efficacy

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2022, VOL. 18, NO. 7, e2145102 (13 pages)
https://doi.org/10.1080/21645515.2022.2145102

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RESEARCH ARTICLE

OPEN ACCESS Check for updates

Safety and efficacy of immune checkpoint inhibitors in advanced cancer patients with autoimmune disease: A meta-analysis

Qi Cai*, Geng-wei Huo*, Fu-yi Zhu*, Ping Yue, Dong-qi Yuan, and Peng Chen

Department of Thoracic Oncology, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin's Clinical Research Center for Cancer, Tianjin Lung Cancer Center, Key Laboratory of Cancer Immunology and Biotherapy, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China

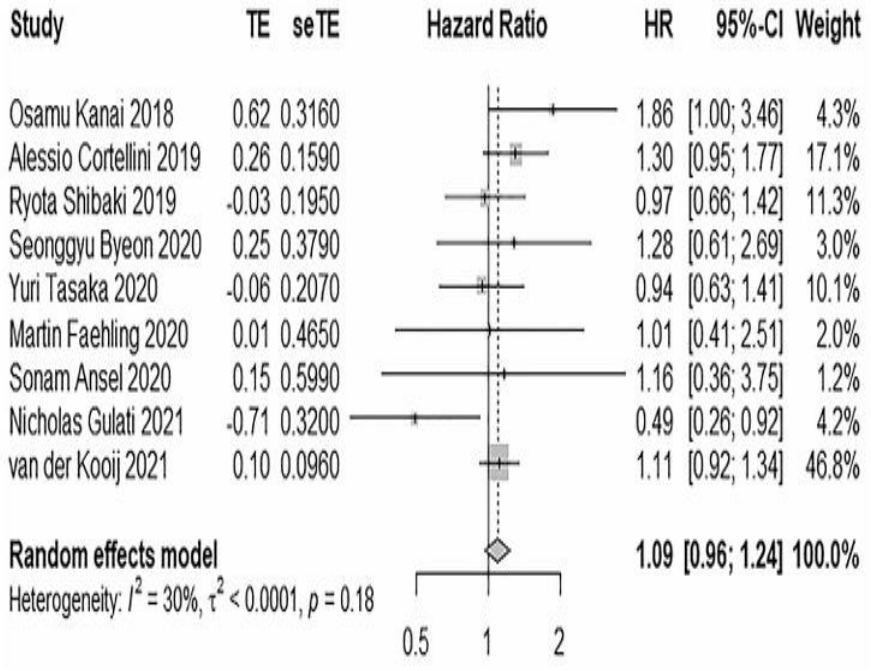

Figure 10. Forest plot of PFS in patients with and without AID receiving ICIs.

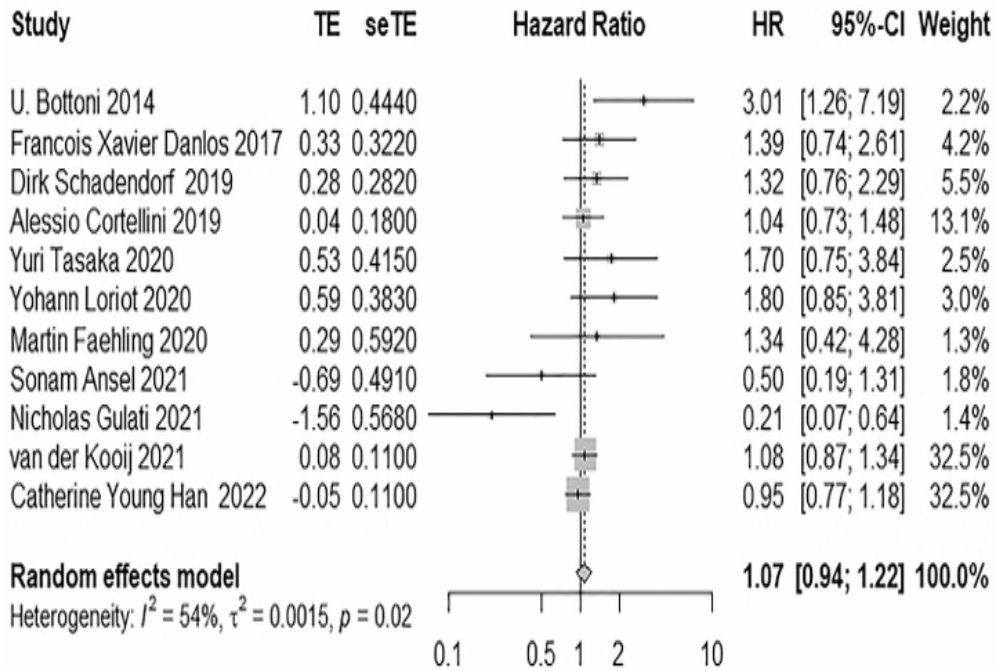

Figure 11. Forest plot of OS in patients with and without AID receiving ICIs.

1ο περιστατικό

- Άνδρας 50 ετων με ca πνευμονα(αδενοκαρκίνωμα).
- PET/CT : ΔΕ πνευμονα, λεμφαδενοπάθεια μεσοθωρακίου και βλάβη αρ επινεφρίδιο.
- PDL-1=1%

- Θεραπεία : carboplatin-pemetrexed-pembrolizumab (6/04/2022-20/06/2022) pembrolizumab 6/2022-12/2024.
- 1/2023 αρθρίτιδα δε καρπού.
- Χορήγηση 10mg πρενδιζολόνης
- Έναρξη μεθοτρεξάτης 4/2023.

2ο περιστατικό

- Άνδρας 70 ετών με ca πνευμονα(αδενοκαρκίνωμα)
- Έκταση νοόσου : Αρ άνω λοβό και αρ κάτω λοβό πνευμονα, λεμφαδενοπάθεια μεσοθωρακίου, και οστικές εντοπίσεις.(PDL-1<1%)
- Έναρξη αγωγής : carboplatin-pemetrexed-pembrolizumab 9/2021-12/2021

  pemetrexed-pembrolizumab 1/2022-8/2022

  pembrolizumab 9/2022-6/2023

1/2022 τυπική εικόνα ρευματικής πολυμυαλγίας.

Χορήγηση 10mg πρενδιζολόνης και συνέχιση αντικαρκινικής θεραπείας με πλήρη ύφεση της ρευματικής πολυμυαλγίας.

6/2022 υποτροπή ρευματικής πολυμυαλγίας και συμμετρική αρθρίτιδα στις πηχεοκαρπικές αρθρώσεις.

2ο περιστατικό

- Διακοπή ανοσοθεραπείας για 2 εγχύσεις.
- προσθήκη μεθοτρεξάτης και επαναχορήγηση ανοσοθεραπείας.
- Απεικονιστικός έλεγχος 4/2025 με σταθερότητα της ογκολογικής νόσου.

3ο περιστατικό

- Ανδρας 71 ετών με ca ουροδόχου με πνευμονικές εντοπίσεις.
- Έναρξη αγωγής με pembrolizumab-enfortumab vedotin(έναντι Νεκτινη 4).
- 5ο κύκλο θεραπείας : Δερματική ψώριαση σε κάτω άκρα και παλάμες, βλεννογονίτιδα στοματικής κοιλότητας.

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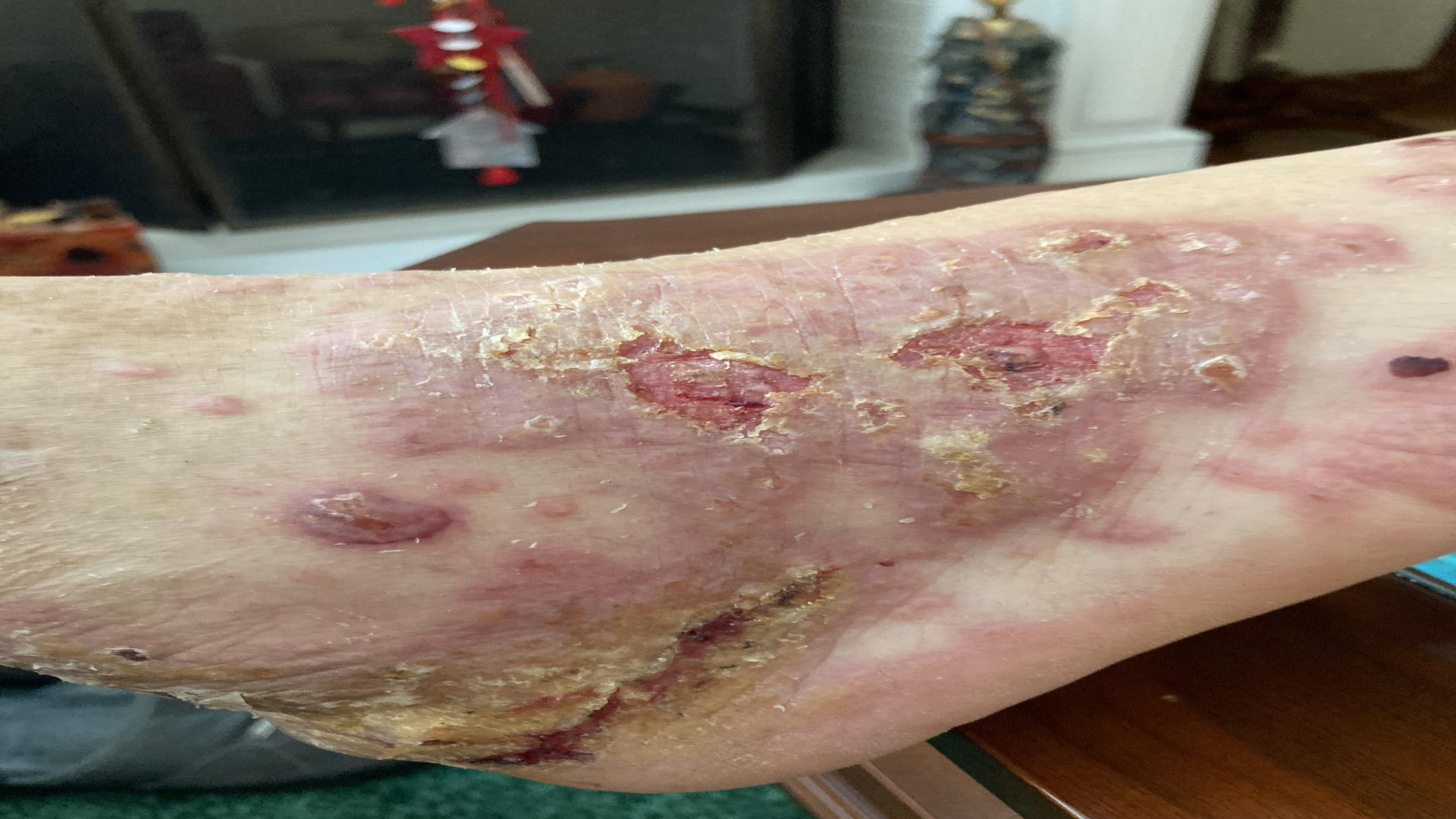
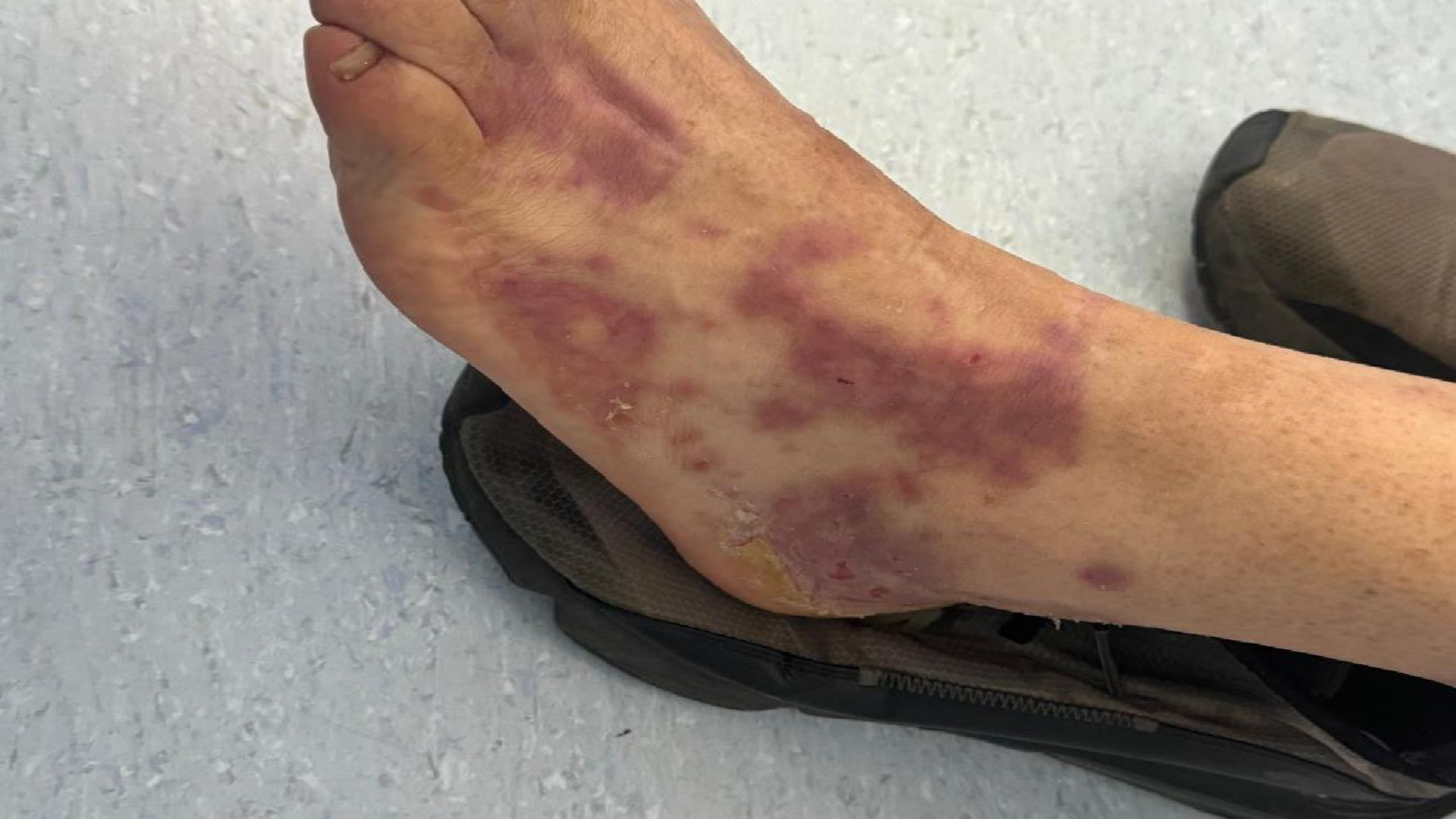


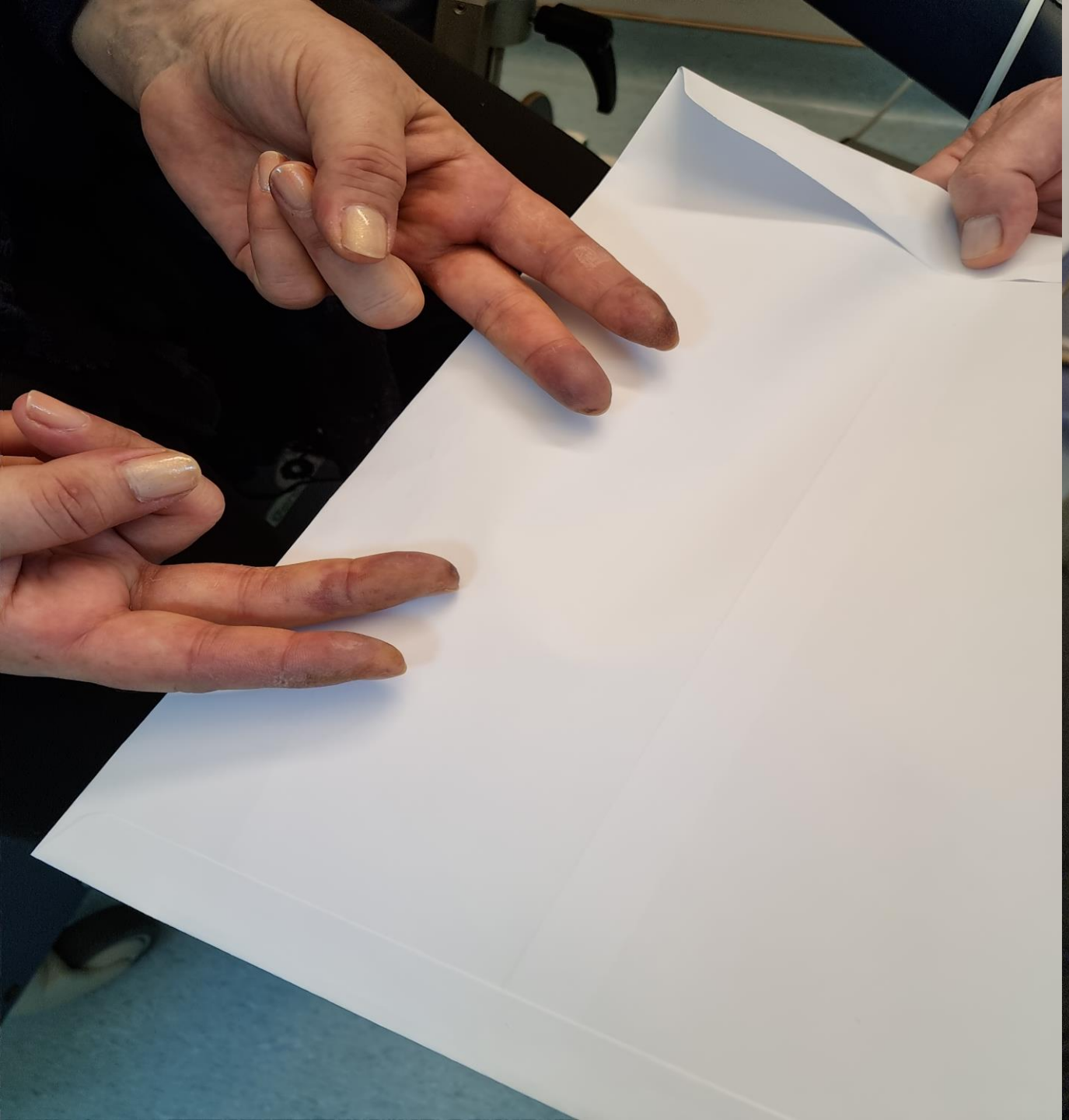
3ο περιστατικό

- Σκέψη για χορήγηση μεθοτρεξάτης....όμως τοπική θεραπεία και διακοπή enfortumab vedotin.
- Συνέχιση ανοσοθεραπείας .



4ο περιστατικό

- Γυναίκα 70 ετών με ca πνευμονα.(PDL1 -)
- Έκταση νόσου : ΔΕ κάτω λοβό πνευμονα ,επινεφρίδια ,οστικές εντοπίσεις.
- Εναρξη χημειοθεραπείας 12/2017
- Προσθήκη pembrolizumab 9/2018-10/2021
- 10/2021.....άλγος και κυάνωση δακτύλων.



5ο περιστατικό

- Αντρας 70 ετών με οροθετική ρευματοειδή αρθρίτιδα υπο μεθοτρεξάτη και adalimumab.
- ca πνευμονα μικροκυτταρικό(περιορισμένο)
- Έναρξη θεραπειας: carboplatin-etoposide-durvalumab(χορήγηση ανοσοθεραπείας για 2 χρόνια).

Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update

Bryan J. Schneider, MD[1]; Jarushka Naidoo, MD[2,3]; Bianca D. Santomasso, MD, PhD[4]; Christina Lacchetti, MHSc[5]; Sherry Adkins, MS[6]; Milan Anadkat, MD[7]; Michael B. Atkins, MD[8]; Kelly J. Brassil, PhD[6]; Jeffrey M. Caterino, MD, MPH[9]; Ian Chau, MD[10]; Marianne J. Davies, DNP[11]; Marc S. Ernstoff, MD[12]; Leslie Fecher, MD[1]; Monalisa Ghosh, MD[13]; Ishmael Jaiyesimi, DO, MS[14]; Jennifer S. Mammen, MD, PhD[15]; Aung Naing, MD[6], Loretta J. Nastoupil, MD[6]; Tanyanika Phillips, MD[16]; Laura D. Porter, MD[17]; Cristina A. Reichner, MD[18]; Carole Seigel, MBA[19], Jung-Min Song, MSN, RN, CNS[20]; Alexander Spira, MD, PhD[21]; Maria Suarez-Almazor, MD[6]; Umang Swami, MD[22]; John A. Thompson, MD[23]; Praveen Vikas, MD[24]; Yinghong Wang, MD[6]; Jeffrey S. Weber, MD, PhD[25]; Pauline Funchain, MD[20]; and Kathryn Bollin, MD[26]

Grading	Management
All grades	Clinicians should follow reports of new joint pain to determine if IA is present. Question whether symptoms new since receiving ICPi.
G1: Mild pain with inflammation, erythema, or joint swelling	Continue ICPi. Initiate analgesia with acetaminophen and/or NSAIDs.
G2: Moderate pain associated with signs of inflammation, erythema, or joint swelling; limiting instrumental ADL	Consider holding ICPi. Escalate analgesia and consider higher doses of NSAIDS as needed. If inadequately controlled, initiate prednisone 10-20 mg/d or equivalent. If improvement, slow taper according to response during the next 4-6 weeks. If no improvement after initial 4 weeks treat as G3. If unable to lower corticosteroid dose to below 10 mg/d after 6-8 weeks, consider DMARD. Consider intra-articular steroid injections for large joints. Referral to rheumatology.
G3-4: Severe pain associated with signs of inflammation, erythema, or joint swelling; irreversible joint damage; disabling; and limiting self-care ADL	Hold ICPi temporarily and may resume in consultation with rheumatology, if recover to ≤ G1. Initiate oral prednisone 0.5-1 mg/kg. If failure of improvement after 2 weeks or worsening in meantime, consider synthetic or biologic DMARD. Synthetic: methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine alone or in combination. Biologic: Consider anticytokine therapy such as TNFα or IL-6 antagonists. Note: As a caution, IL6 inhibition can cause intestinal perforation.[141] Although this is extremely rare, it should not be used in patients with concomitant immune-related colitis. Referral to rheumatology.
Additional considerations Early recognition is critical to avoid erosive joint damage. Corticosteroids can be used as part of initial therapy in IA, but because of likely prolonged treatment requirements, physicians should consider starting steroid-sparing agents earlier than one would with other irAEs. Oligoarthritis can be treated early on with intra-articular steroids, consider early referral.	

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Management of toxicities from immunotherapy: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

J. Haanen[1†], M. Obeid[2,3,4†], L. Spain[5,6,7], F. Carbonnel[8,9], Y. Wang[10], C. Robert[11,12], A. R. Lyon[13,14], W. Wick[15,16], M. Kostine[17], S. Peters[4], K. Jordan[18,19] & J. Larkin[20], on behalf of the ESMO Guidelines Committee*

Symptom grade	Assessment and investigations	Management escalation pathway
Grade 1: mild pain, stiffness and/or weakness	Document joint or muscle inflammation: joint swelling, ESR, CRP, CK level, X-ray and US of affected joints, analysis of synovial fluid if possible; consider autoimmune blood panel, including ANAs, RF, anti-CCP and consider HLA-B27 testing if spine affected[a]	Continue ICI therapy Start analgesics and/or NSAIDs Refer to rheumatologist if no improvement in arthralgia [IV, B]
Grade 2: moderate pain, stiffness and/or weakness limiting instrumental ADL	Refer to rheumatologist Assessments and investigations as for grade 1 In case of no response, consider imaging (US, MRI, CT scan) of refractory arthritis and suspicion of metastatic lesions or septic arthritis Consider ANCA and imaging (PET–CT) for refractory PMR	Arthralgia: • As for grade 1 Inflammatory arthritis-PMR [IV, A]:[b] • Continue ICI therapy • Start prednisone or equivalent 10–20 mg/day and consider higher dosage (0.5 mg/kg/day) if no improvement • Consider intra-articular CSs if mono- or oligoarthritis • Response: progressively taper CSs • No response: consider hydroxychloroquine, sulfasalazine, methotrexate (consider IL-6R or TNF-α inhibitor if no clinical improvement) Myositis [IV, A]:[c] • Withhold ICI therapy • Start prednisone at 0.5–1 mg/kg/day or equivalent • Response: progressively taper CSs • No response: if severe disease,[d] consider methotrexate, azathioprine, MMF, tacrolimus or IL-6R inhibitor; consider TNF-α inhibitor if fasciitis with or without eosinophilia
Grade 3: severe pain, stiffness and/or weakness limiting self-care ADL	Refer to rheumatologist Assessments and investigations as for grades 1 and 2	Inflammatory arthritis-PMR [IV, A]: • As for grade 2, but temporarily withhold ICI therapy Myositis [IV, A]: • Withhold ICI therapy • Consider hospitalisation and start prednisone at 1 mg/kg/day or equivalent and i.v. pulses of methylprednisolone (2 mg/kg or higher) ± IVIG ± plasma exchange in life-threatening manifestations • Treat response or no response as for grade 2
Grade 4: life-threatening consequences	Refer to rheumatologist Assessments and investigations as for grades 1 and 2	Inflammatory arthritis-PMR [IV, A]: • Withhold ICI therapy and consider IL-6R inhibitor (preferred) or TNF-α inhibitor if no response to prednisone 0.5 mg/kg/day Myositis [IV, A]: • As for grade 3

EULAR points to consider for the diagnosis and management of rheumatic immune-related adverse events due to cancer immunotherapy with checkpoint inhibitors

Marie Kostine ,[1] Axel Finckh ,[2] Clifton O Bingham 3rd,[3] Karen Visser,[4] Jan Leipe,[5,6] Hendrik Schulze-Koops,[6] Ernest H Choy,[7] Karolina Benesova,[8] Timothy R D J Radstake,[9] Andrew P Cope,[10] Olivier Lambotte,[11] Jacques-Eric Gottenberg ,[12] Yves Allenbach ,[13] Marianne Visser,[14] Cindy Rusthoven,[14] Lone Thomasen,[15] Shahin Jamal,[16] Aurélien Marabelle,[17] James Larkin,[18] John B A G Haanen,[19] Leonard H Calabrese ,[20] Xavier Mariette,[21,22] Thierry Schaeverbeke[1]

Immune-Related Adverse Events by Immune Checkpoint Inhibitors Significantly Predict Durable Efficacy Even in Responders with Advanced Non-Small Cell Lung Cancer

Hiroaki Akamatsu,[a] Eriko Murakami,[a] Jun Oyanagi,[a] Ryota Shibaki,[a] Takahiro Kaki,[a] Eri Takase,[a] Masanori Tanaka,[a] Yuhei Harutani,[a] Nao Yamagata,[a] Yuka Okuda,[a] Katsuyuki Furuta,[a] Takeya Sugimoto,[a] Shunsuke Teraoka,[a] Atsushi Hayata,[a] Nahomi Tokudome,[a] Yuichi Ozawa,[a] Keita Mori,[b] Yasuhiro Koh,[a] Nobuyuki Yamamoto[a]

[a]Internal Medicine III, Wakayama Medical University, Wakayama City, Wakayama, Japan; [b]Clinical Trial Management Department, Shizuoka Cancer Center, Shizuoka, Japan

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Immune-related adverse event • Immune checkpoint inhibitor • Predictive marker

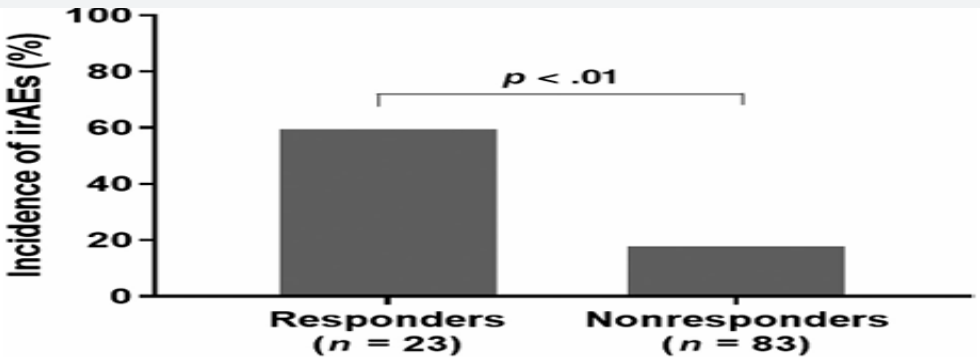


Figure 1. Proportion of those who had at least one immune-related adverse event between responders (n = 23) and nonresponders (n = 83).
Abbreviation: irAEs, immune-related adverse events.

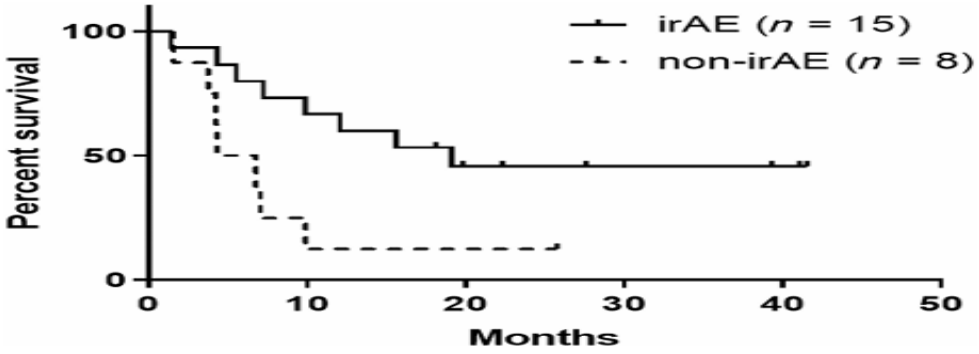


Figure 2. Kaplan–Meier curve of progression-free survival (bold line: irAE group [n = 15]; dashed line: no-irAE group [n = 8]).
Abbreviation: irAE, immune-related adverse event.

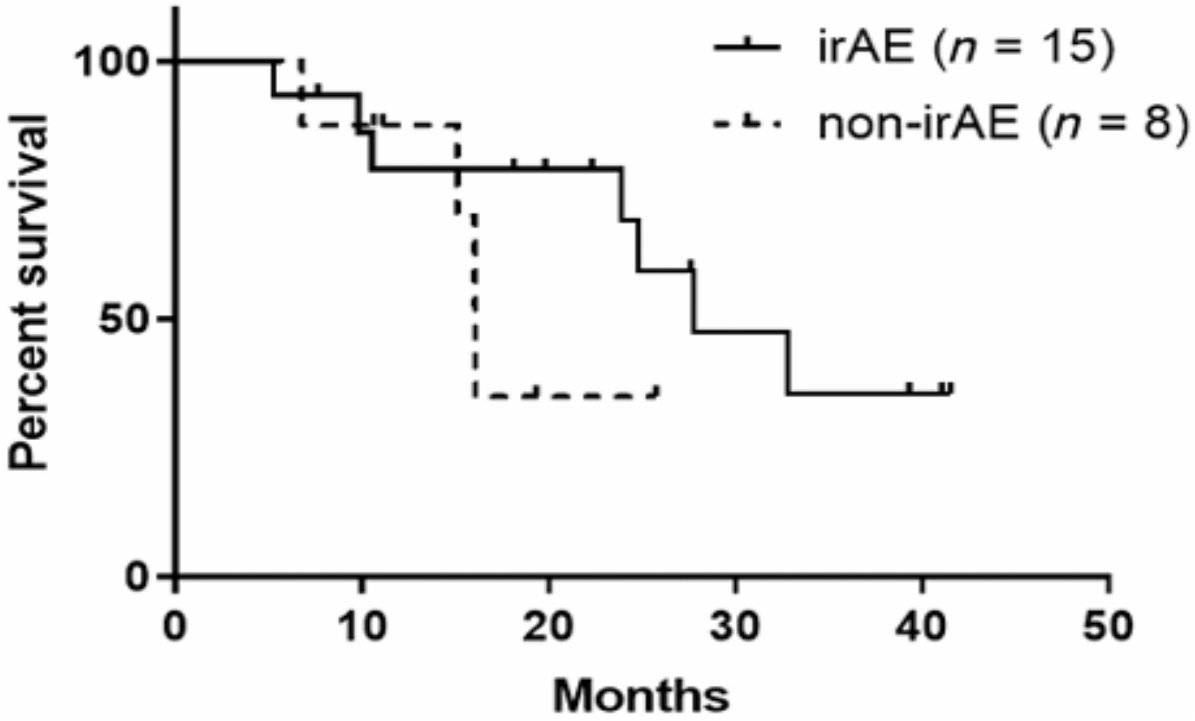


Figure 4. Kaplan-Meier curve of overall survival (bold line: irAE group [n = 15]; dashed line: no-irAE group [n = 8]).
Abbreviation: irAE, immune-related adverse event.

Immune-Related Adverse Events as Clinical Biomarkers in Patients with Metastatic Renal Cell Carcinoma Treated with Immune Checkpoint Inhibitors

Dylan J. Martini,[a,b] Subir Goyal,[c] Yuan Liu,[c] Sean T. Evans,[b,d] T. Anders Olsen,[b,d] Katherine Case,[b,d] Benjamin L. Magod,[b,g] Jacqueline T. Brown,[b,d] Lauren Yantorni,[b] Greta Anne Russler,[b] Sarah Caulfield,[d,e] Jamie M. Goldman,[b,d] Bassel Nazha,[b,d] Wayne B. Harris,[b,d] Haydn T. Kissick,[f] Viraj A. Master,[f] Omer Kucuk,[b,d] Bradley C. Carthon,[b,d] Mehmet Asim Bilen[b,d]

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Immune checkpoint inhibitors • Renal cell carcinoma • Immune-related adverse events • Clinical biomarkers • Clinical outcomes

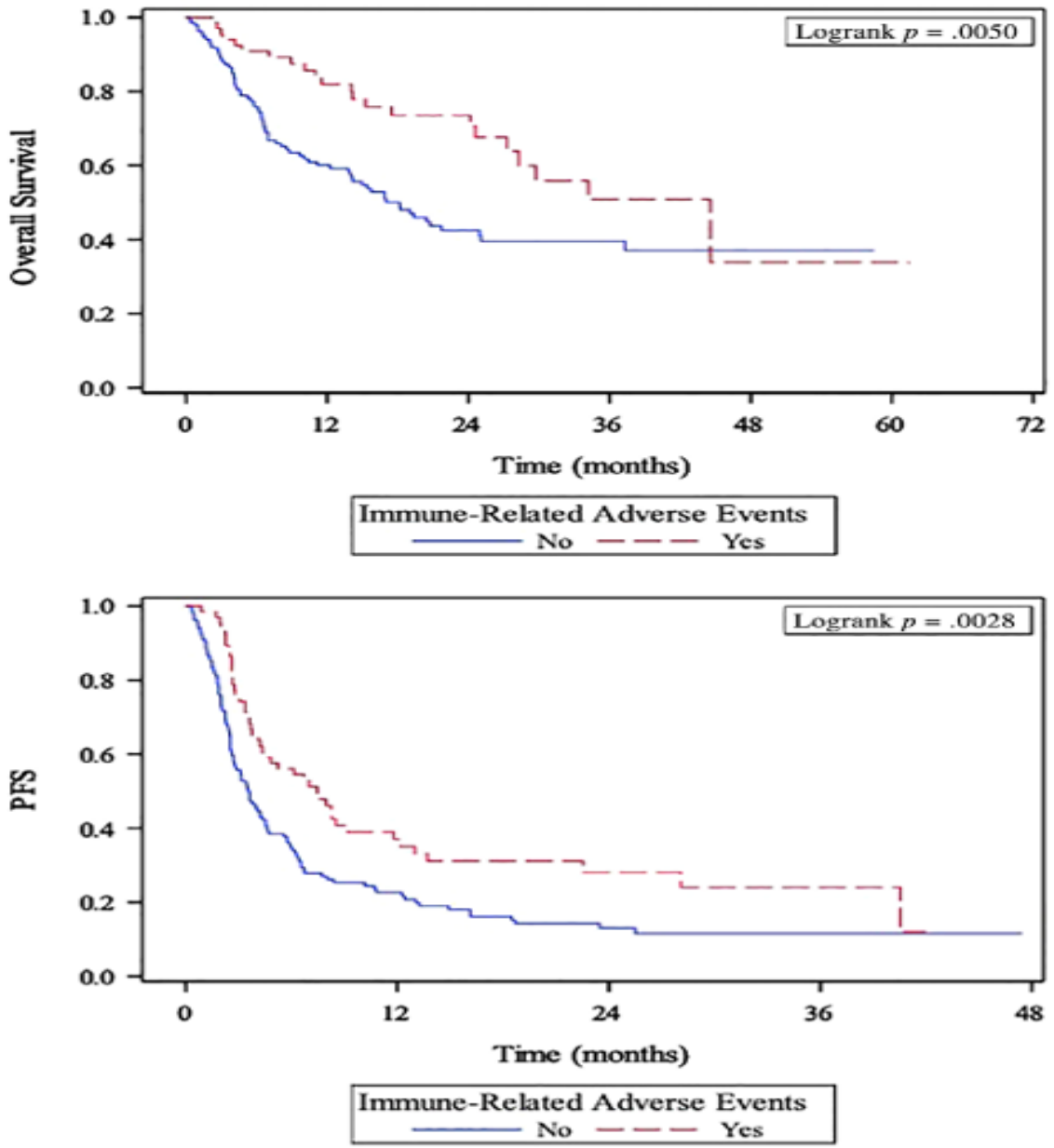

Figure 1. Kaplan-Meier curves of association between immune-related adverse events and overall survival (top panel) and progression-free survival (bottom panel).
Abbreviation: PFS, progression-free survival.

European Journal of Cancer 207 (2024) 114172

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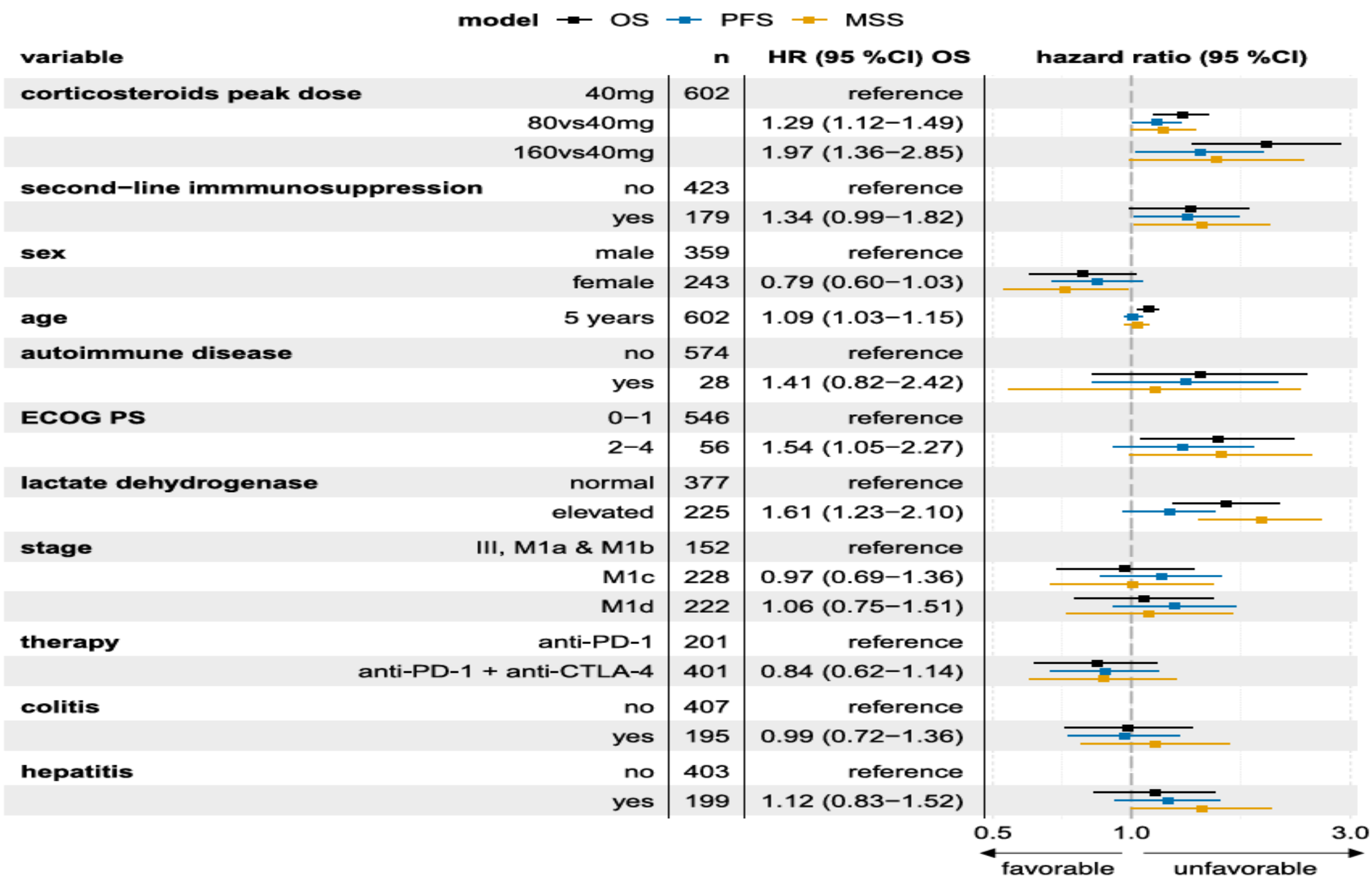
journal homepage: www.ejcancer.com

Corticosteroids and other immunosuppressants for immune-related adverse events and checkpoint inhibitor effectiveness in melanoma☆

Rik J. Verheijden [a,b], Femke H. Burgers [c], Josephine C. Janssen [d], Anouk E. Putker [e], Sophie P.G. R. Veenstra [f], Geke A.P. Hospers [g], Maureen J.B. Aarts [h], Karel W. Hehenkamp [i], Veerle L. E. Doornebosch [j], Marthe Verhaert [k], Franchette W.P.J. van den Berkmortel [l], Katerina Chatzidionysiou [m], Arturo Llobell [n], Milton Barros [o], Alexandre T.J. Maria [p], Akari Takeji [q], José-Salvador García Morillo [r], Merav Lidar [s], Mick J.M. van Eijs [a,t], Christian U. Blank [u], Sandrine Aspeslagh [k], Djura Piersma [j], Ellen Kapiteijn [i], Mariette Labots [f], Marye J. Boers-Sonderen [e], Astrid A.M. van der Veldt [v], John B.A.G. Haanen [c,i,w], Anne M. May [b], Karijn P.M. Suijkerbuijk [a,*]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variable
n
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hazard ratio (95 %CI)
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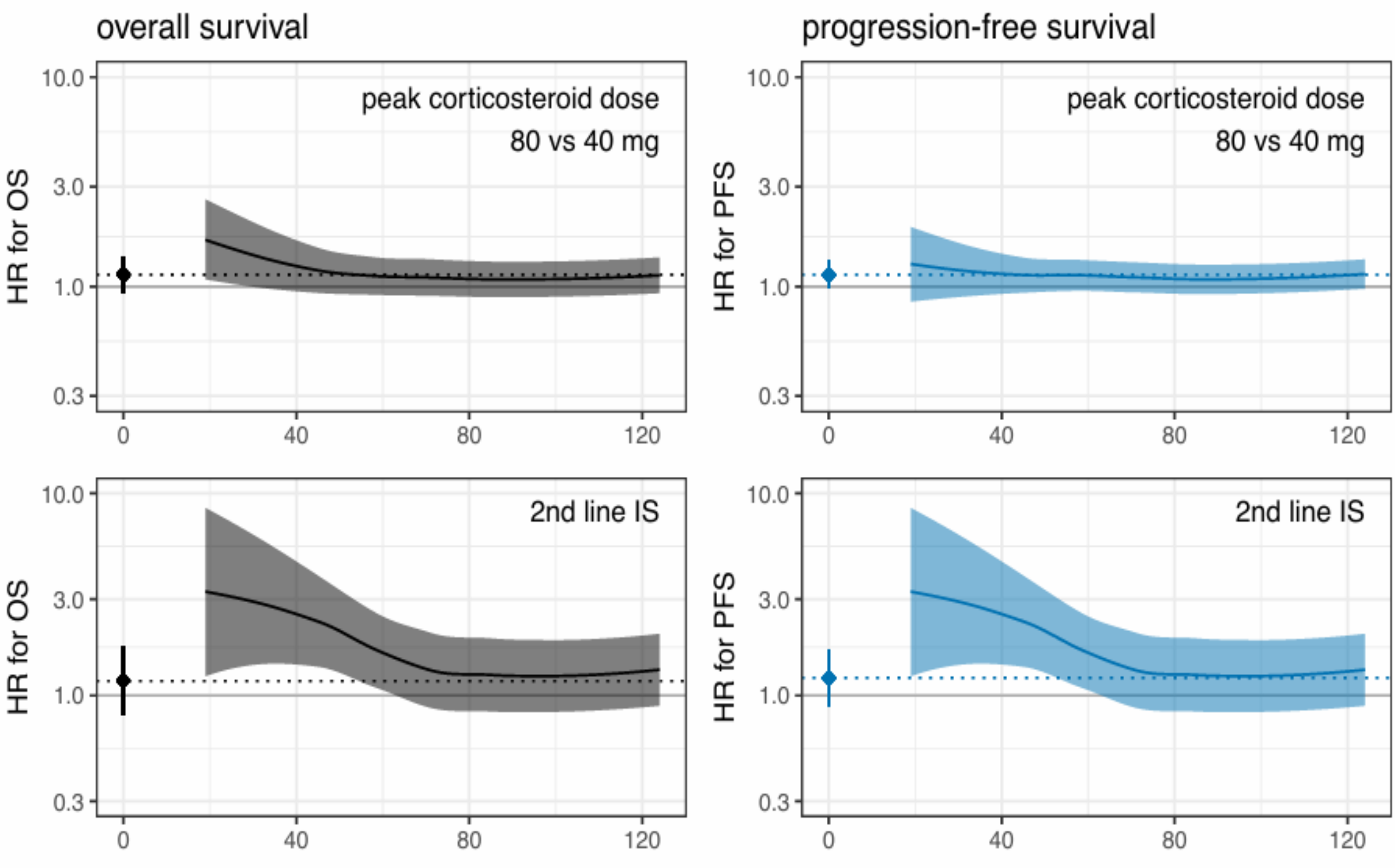
80vs40mg 1.29 (1.12–1.49)
160vs40mg 1.97 (1.36–2.85)
second−line immmunosuppression
no 423 reference
yes 179 1.34 (0.99–1.82)
sex
male 359 reference
female 243 0.79 (0.60–1.03)
age
5 years 602 1.09 (1.03–1.15)
autoimmune disease
no 574 reference
yes 28 1.41 (0.82–2.42)
ECOG PS
0–1 546 reference
2–4 56 1.54 (1.05–2.27)
lactate dehydrogenase
normal 377 reference
elevated 225 1.61 (1.23–2.10)
stage
III, M1a & M1b 152 reference
M1c 228 0.97 (0.69–1.36)
M1d 222 1.06 (0.75–1.51)
therapy
anti-PD-1 201 reference
anti-PD-1 + anti-CTLA-4 401 0.84 (0.62–1.14)
colitis
no 407 reference
yes 195 0.99 (0.72–1.36)
hepatitis
no 403 reference
yes 199 1.12 (0.83–1.52)
0.5
1.0
3.0
favorable
unfavorable


overall survival
progression-free survival
peak corticosteroid dose
80 vs 40 mg
2nd line IS
HR for OS
HR for PFS
10.0
3.0
1.0
0.3
0
40
80
120

Συμπερασματικά....

- Ναι στη χορήγηση ανοσοθεραπείας σε ασθενείς με ήδη αυτοάνοσο νόσημα.
- Αντιμετώπιση της τυχόν υποτροπής η της ανοσοεπαγώμενης ανεπιθύμητης με ήπια θεραπεία.
- Συνήθως δεν είναι αναγκαία η χρήση βιολογικού παράγοντα.
- Η χαμηλή δόση κορτικοειδούς και μεθοτρεξάτης επιτρέπει την συνεχιση ανοσοθεραπείας στους ασθενείς με ογκολογικό νόσημα .


ΣΑΣ ΕΥΧΑΡΙΣΤΩ