Περιστατικό με CPI και Αρθρίτιδα

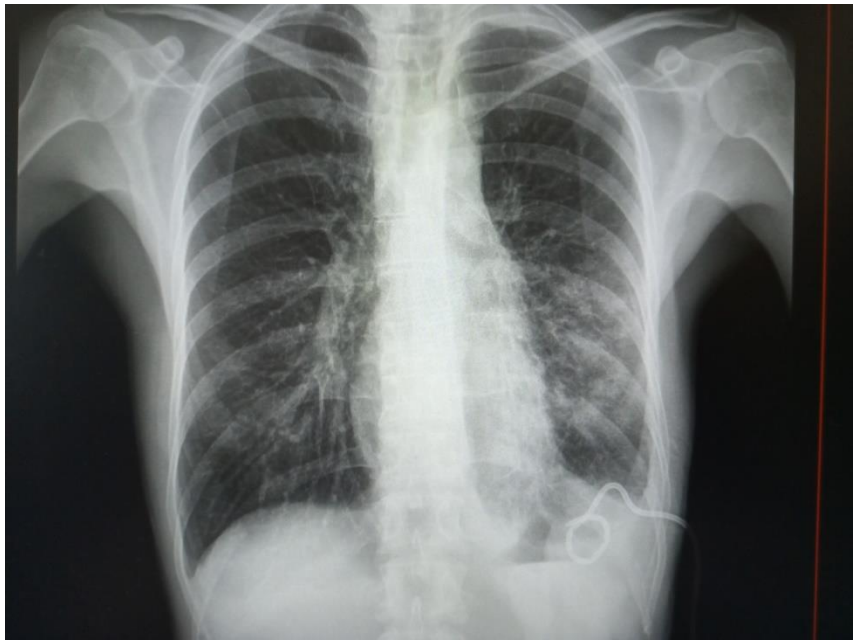
Γεώργιος Δεμιρτζόγλου

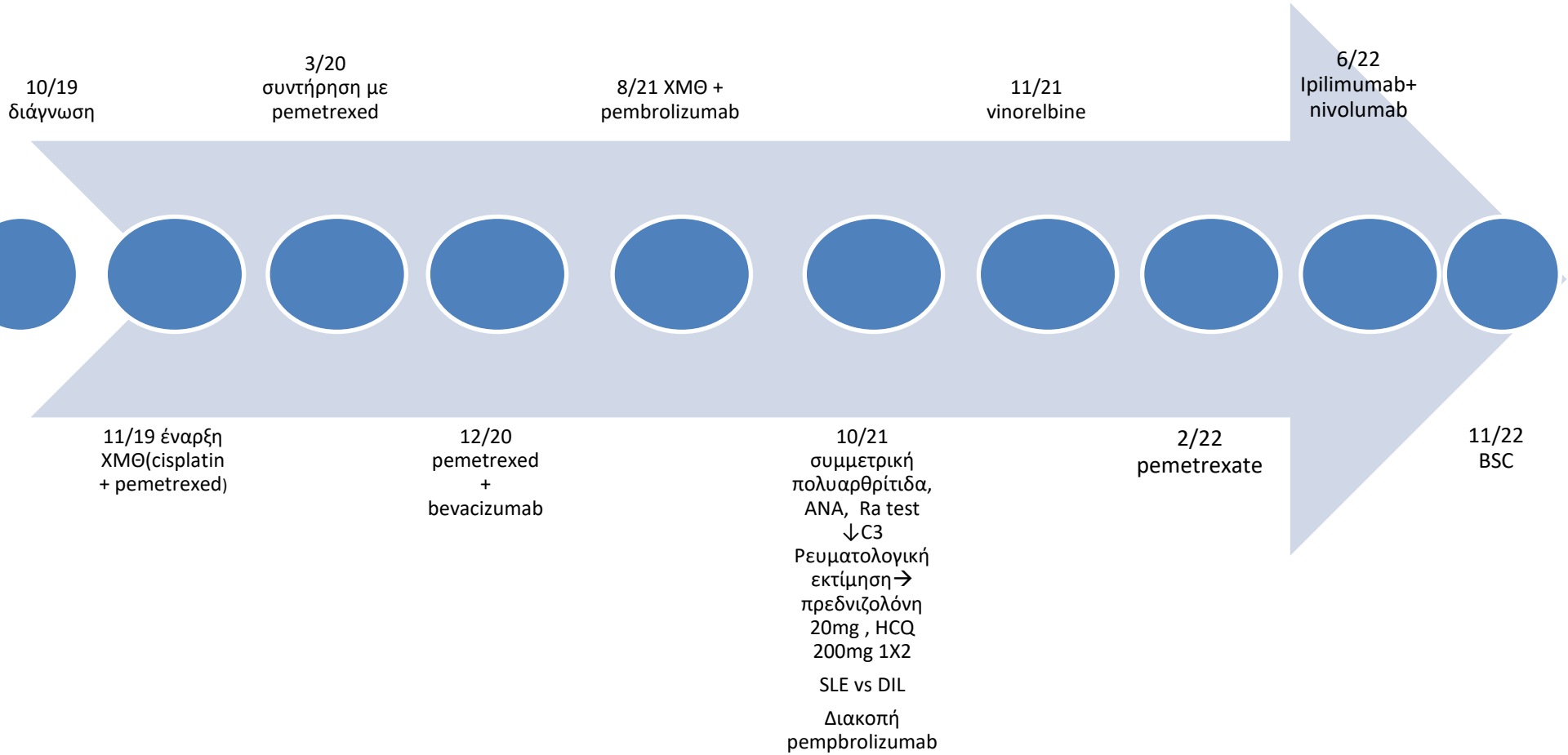
Ρευματολογική κλινική 251 ΓΝΑ

Δεν υπάρχει καμία σύγκρουση συμφερόντων

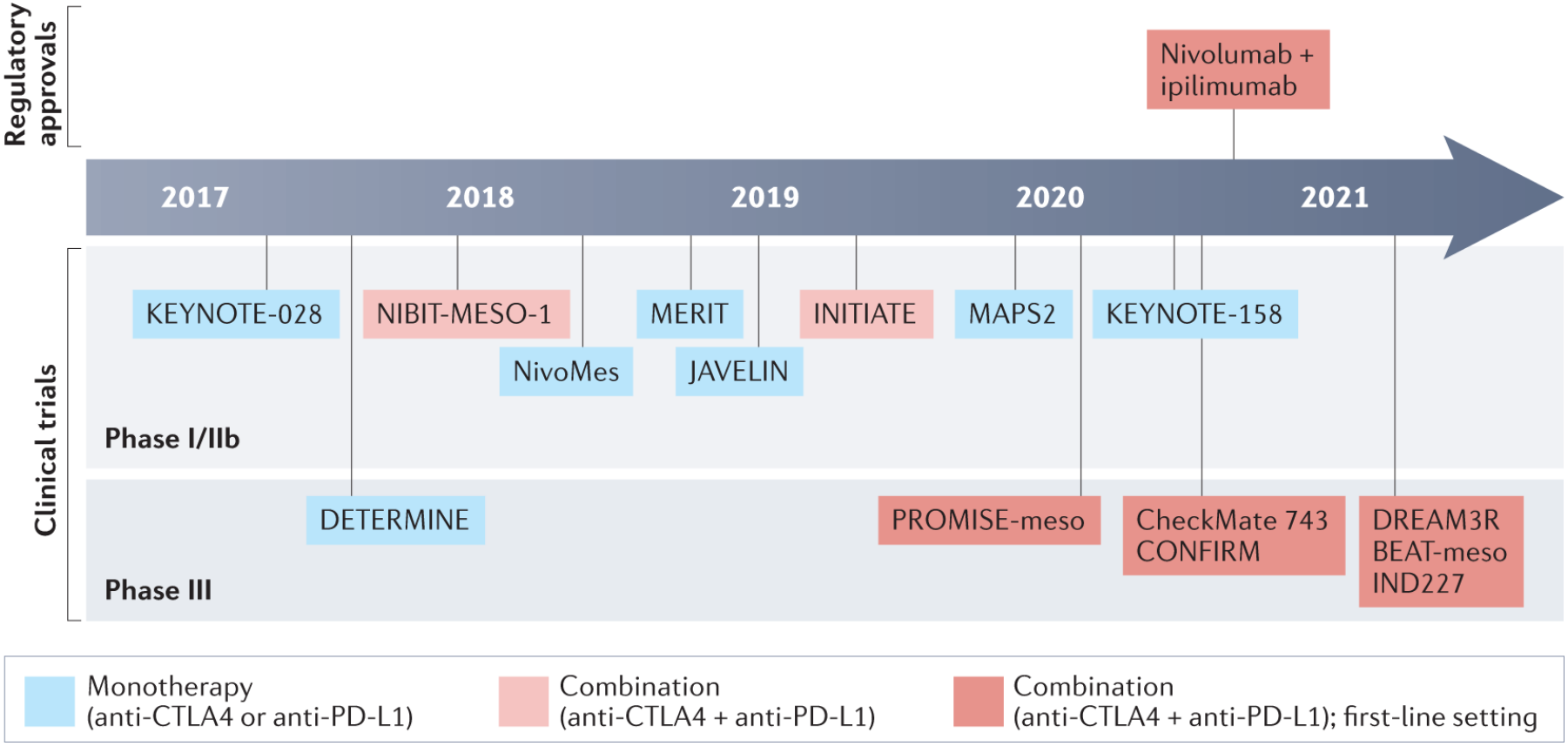
Παρουσίαση περιστατικού

- 45 ετών ♀ με βήχα, δύσπνοια
- α/α υποθυρεοειδισμός
- Πλευριτική συλλογή αριστερά → διερεύνηση στην πνευμονολογική κλινική
- Βιοψία υπεζωκότα → μεσοθηλίωμα
- PET –CT→ πάχυνση υπεζωκότα αριστερά και πολλαπλοί παθολογικοί λεμφαδένες (μεσοθωράκιο , υπερκλείδιες χώρες και άνω κοιλία)



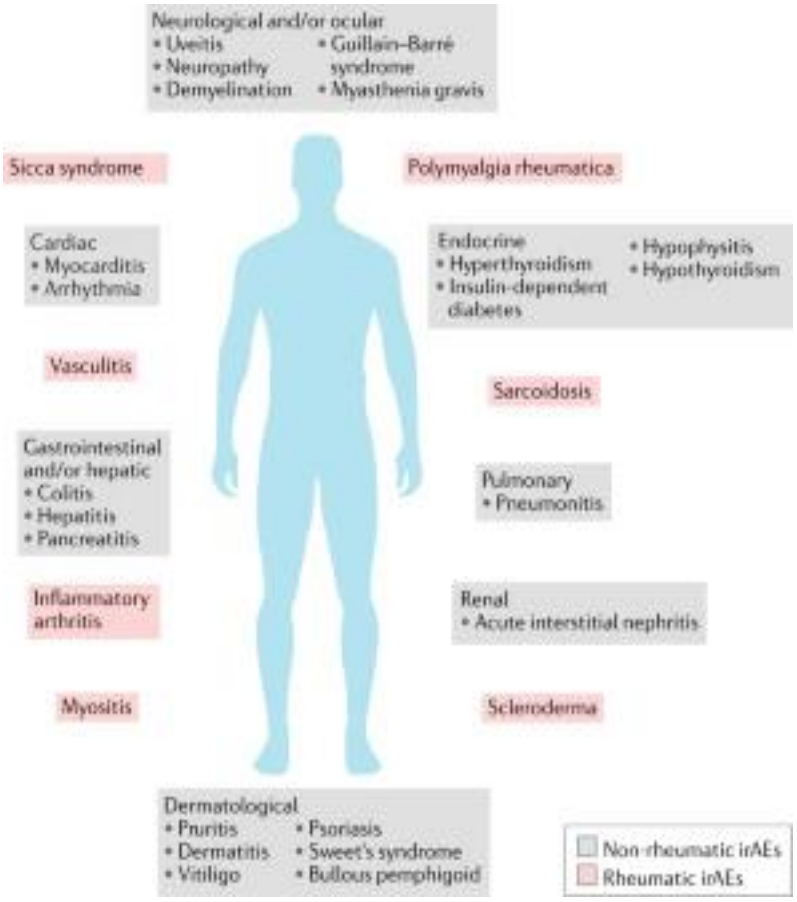

10/19
διάγνωση
11/19 έναρξη
ΧΜΘ(cisplatin
+ pemetrexed)
3/20
συντήρηση με
pemetrexed
12/20
pemetrexed
+
bevacizumab
8/21 ΧΜΘ +
pembrolizumab
10/21
συμμετρική
πολυαρθρίτιδα,
ANA, Ra test
↓C3
Ρευματολογική
εκτίμηση→
πρεδνιζολόνη
20mg , HCQ
200mg 1X2
SLE vs DIL
Διακοπή
pempbrolizumab
11/21
vinorelbine
2/22
pemetrexate
6/22
Ipilimumab+
nivolumab
11/22
BSC

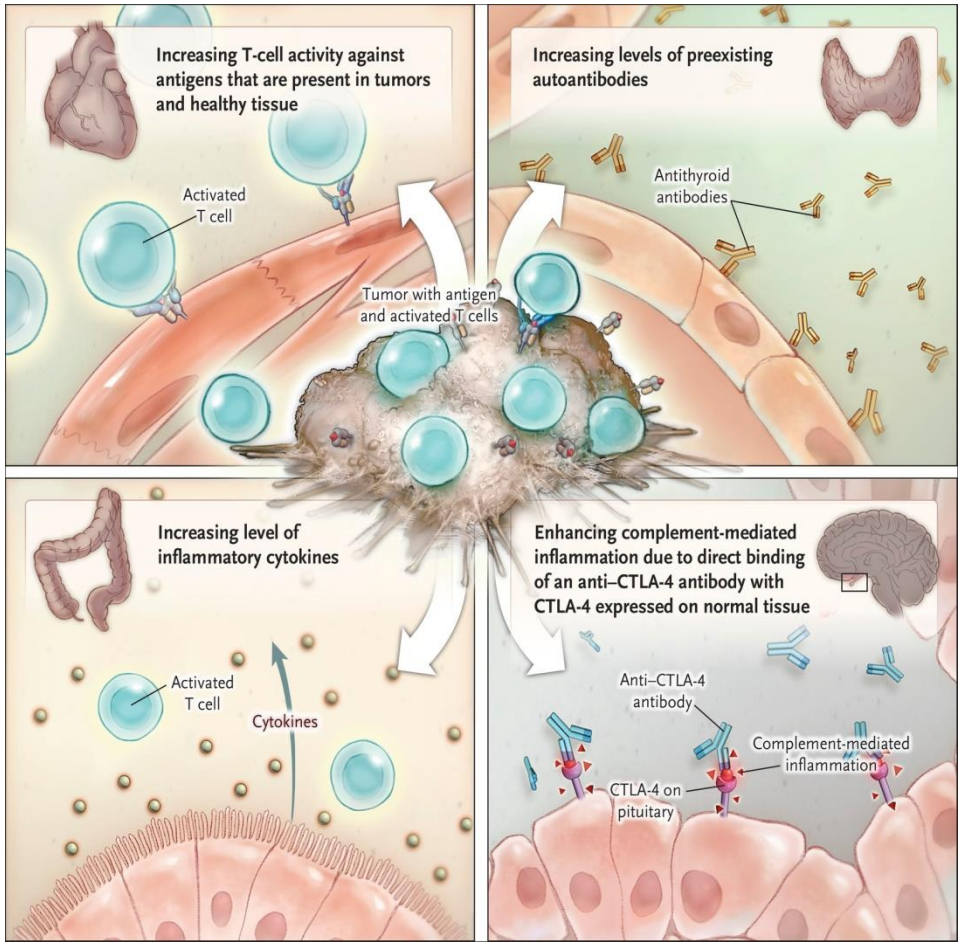
CPI στο μεσοθηλίωμα



Fennell, D.A., Dulloo, S. & Harber, J. Immunotherapy approaches for malignant pleural mesothelioma. Nat Rev Clin Oncol 19, 573–584 (2022). https://doi.org/10.1038/s41571-022-00649-7

Ανεπιθύμητες ενέργειες από CPI





Calabrese, L.H., Calabrese, C. & Cappelli, L.C. Rheumatic immune-related adverse events from cancer immunotherapy. Nat Rev Rheumatol 14, 569–579 (2018). https://doi.org/10.1038/s41584-018-0074-9

Postow, Michael A et al. "Immune-Related Adverse Events Associated with Immune Checkpoint Blockade." The New England journal of medicine vol. 378,2 (2018): 158-168. doi:10.1056/NEJMra1703481

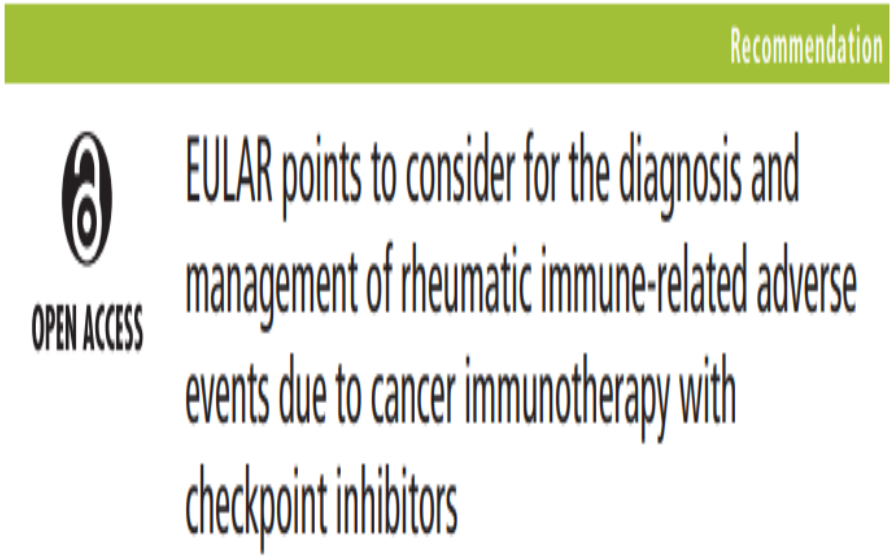
Αρθρίτιδα από CPI

- Αρθρίτιδα →5-10% των ασθενών που λαμβάνουν CPI
- Συχνότερη σε PD-1/PD-L1 αναστολείς
- Εκδήλωση κατά μέσο όρο 120 ημέρες από την λήψη του φαρμάκου
- Εκδήλωση ως μονο, ολιγο, πολυαρθρίτιδα, αντιδραστική αρθρίτιδα , ψωριασική αρθρίτιδα ,
- Συχνότερα πολυαρθρίτιδα
- Μπορεί να είναι διαβρωτική (πρώιμα)
- Συνήθως δεν ανευρίσκονται αυτοαντισώματα (9% RF+, 7% Anti-CCP anti-RA33?)
- Εκτίμηση αριθμού προσβεβλημένων αρθρώσεων, TKE, CRP, Ra test, anti-CCP, ANA και ανάλυση αρθρικού υγρού
- Κάθε αρθρίτιδα grade 2, 3,4→ πρώιμη παραπομπής σε ρευματολόγο
- Σοβαρότερη και συχνότερη σε συνδυασμό θεραπειών

Ghosh N, Tiongson MD, Stewart C, et al. Checkpoint Inhibitor-Associated Arthritis: A Systematic Review of Case Reports and Case Series. J Clin Rheumatol. 2021;27(8):e317-e322. doi:10.1097/RHU.0000000000001370

Κατευθυντήριες οδηγίες

Ρευματολόγοι



Kostine M, Finckh A, Bingham CO, et al. EULAR points to consider for the diagnosis and management of rheumatic immune-related adverse events due to cancer immunotherapy with checkpoint inhibitors. Ann Rheum Dis. 2021;80(1):36-48. doi:10.1136/annrheumdis-2020-217139

Ογκολόγοι

Haanen, J. et al Management of toxicities from immunotherapy: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Annals of oncology : official journal of the European Society for Medical Oncology, 33(12), 1217–1238. https://doi.org/10.1016/j.annonc.2022.10.001

Κατευθυντήριες οδηγίες- Ρευματολόγοι

Overarching principles

A.	Rheumatic and musculoskeletal immune-related adverse events can occur as manifestations in cancer patients receiving immunotherapy with checkpoint inhibitors.	n.a.	n.a.	9.6 (0.7)
B.	Management of rheumatic and musculoskeletal immune-related adverse events should be based on a shared decision-making process between patients, oncologists and rheumatologists.	n.a.	n.a.	9.5 (1.1)
C.	Rheumatologists should engage with oncologists to contribute to the inter-disciplinary care of patients presenting with musculoskeletal signs and symptoms.	n.a.	n.a.	9.1 (1.2)
D.	The role of rheumatologists is to assist oncologists in differential diagnosis and to relieve rheumatic and musculoskeletal symptoms to an acceptable level enabling patients to maintain effective cancer immunotherapy.	n.a.	n.a.	9.5 (0.9)

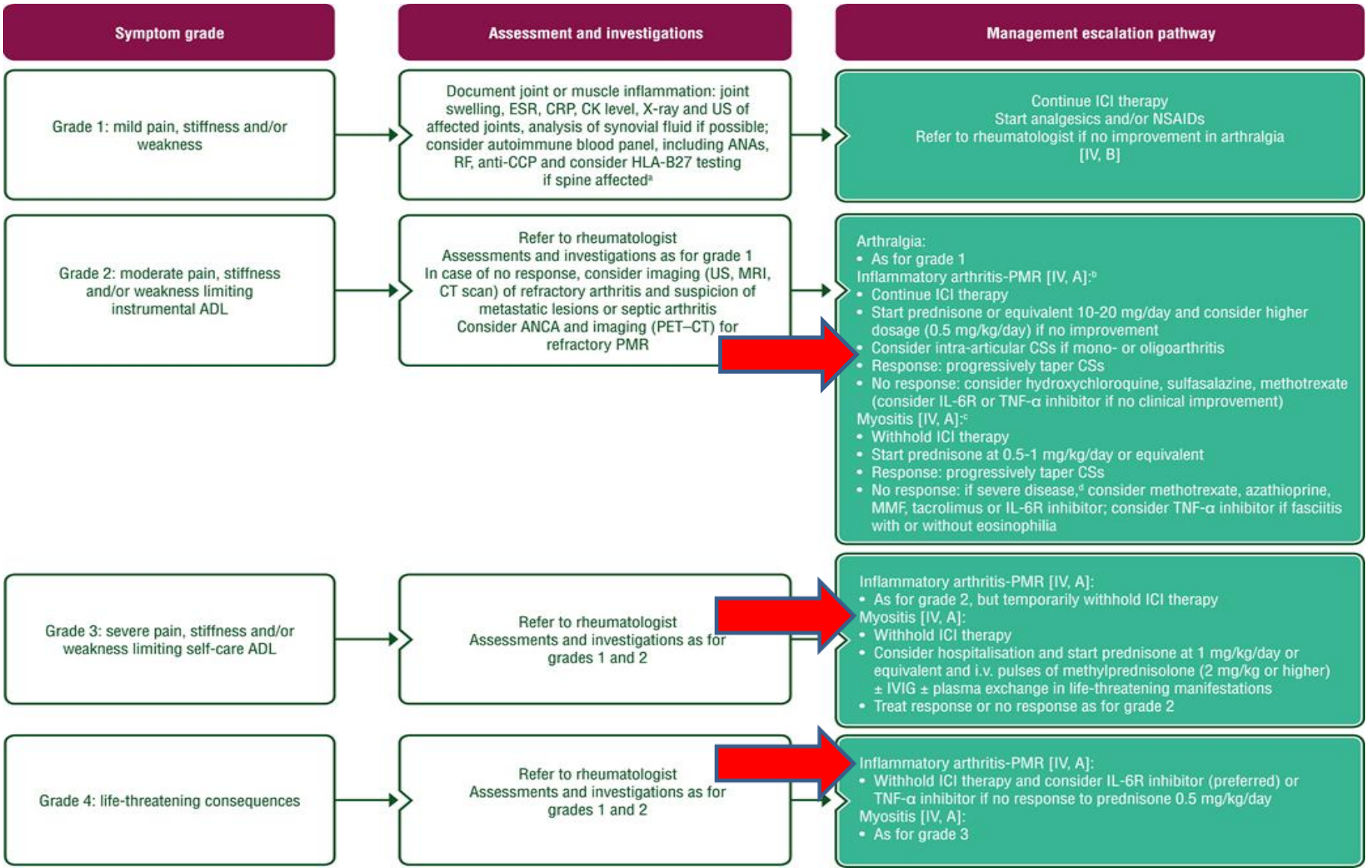
Points to consider

1.	Rheumatologists should be aware of the wide spectrum of clinical presentations of rheumatic and/or systemic immune-related adverse events that often do not fulfil traditional classification criteria of RMDs.	4	C	9.5 (1.2)
2.	Oncologists should be encouraged to consult rheumatologists promptly for assessment when rheumatic musculoskeletal and systemic signs or symptoms are suspected due to immunotherapy, and rheumatologists should provide facilitated access for such patients.	5	D	9.4 (1.3)
3.	Metastases, paraneoplastic syndromes and unrelated rheumatic diseases should be considered as a potential differential diagnosis of rheumatic immune-related events. The comprehensive assessment should be focused on documenting evidence of target organ inflammation, and based on history, clinical features, laboratory tests, imaging and/or biopsy.	4	C	9.5 (0.9)

Κατευθυντήριες οδηγίες- Ρευματολόγοι

4.	In case of inefficacy of symptomatic treatment and depending on the disease severity, local and/or systemic glucocorticoids should be considered for immune-related rheumatic and systemic symptoms. Dose regimen and route of administration should be decided according to the clinical entity and activity. When improvement is achieved, systemic glucocorticoids should be tapered to the lowest effective dose to control the symptoms.	4	C	9.4 (1)
5.	csDMARD should be considered in patients with insufficient response to acceptable dose of glucocorticoids or requiring glucocorticoid-sparing.	4	C	9 (1.2)
6.	For patients experiencing severe immune-related rheumatic and systemic immune-related adverse events or with insufficient response to csDMARD, bDMARD may be considered, with TNF or IL-6 inhibitors being the preferred options for inflammatory arthritis.	4	C	8.8 (1.2)
7.	The decision to hold or to continue the cancer immunotherapy should be based on the severity of rheumatic immune-related adverse events, the extent of required immunosuppressive regimen, the tumour response and its duration, as well as the future oncology treatment plan, in a shared decision with the patient.	5	D	9.4 (1)
8.	Myositis may be a severe condition. Immunotherapy withdrawal needs to be discussed. In the presence of life-threatening manifestations (bulbar symptoms (dysphagia, dysarthria, dysphonia), dyspnoea and myocarditis), high dose of glucocorticoids, IVIg and/or plasma exchange should be considered; immunotherapy withdrawal is always necessary.	4	C	8.9 (1.2)
9.	A pre-existing autoimmune rheumatic and/or systemic disease should not preclude the use of cancer immunotherapy. Baseline immunosuppressive regimen should be kept at the lowest dose possible (for glucocorticoids, below 10 mg prednisone per day if possible). However, many patients may have a flare of the underlying condition and/or immune-related adverse events, requiring the use of glucocorticoids and/or DMARDs.	4	C	9 (1.3)
10.	Before initiation of cancer immunotherapy, there is no indication to test every patient for the presence of autoantibodies. In the case of unexplained rheumatic, musculoskeletal or systemic symptoms, a complete rheumatological assessment should be performed.	5	D	9 (1.3)

Κατευθυντήριες οδηγίες- Ογκολόγοι



CPI σε αυτοάνοσα νοσήματα

Box 2 | Considerations for initiation of immune-checkpoint inhibitors in patients with pre-existing autoimmune disease

Immune-checkpoint inhibitor (ICI) use in a metastatic or adjuvant setting:

- ICIs should be offered to patients with pre-existing autoimmune disease who have metastatic cancer.
- In an adjuvant setting, ICI use should be balanced with consideration of both cancer prognosis and autoimmune-disease characteristics (type, severity, activity).
- Shared decision-making and informed consent is essential.

ICI use as monotherapy or combination therapy:

- The best oncological treatment should always be considered.
- Risk of autoimmune-disease flare or other immune toxicity is higher with combination therapy.
- Case-by-case discussion is advised, ideally within a multidisciplinary board.

Pre-existing autoimmune-disease type:

- A higher rate of flares is reported in patients with psoriatic arthritis, polymyalgia rheumatica or rheumatoid arthritis than in those with other autoimmune conditions.
- Caution is advised for patients with neurological or life-threatening autoimmune disease.
- ICI introduction and its monitoring should be validated within a multidisciplinary board in instances of severe autoimmune disease.

Pre-existing autoimmune-disease activity and ongoing immunosuppressive treatment:

- Evidence is mixed in relation to the risk of immune toxicity in patients with active autoimmune disease at ICI onset.
- Higher risk of immune toxicity is reported in patients with intensive immunosuppressive therapies than in those with less-intensive treatment.
- Autoimmune disease activity should be assessed prior to ICI initiation.
- Monitoring should be adapted to baseline autoimmune-disease activity and severity of previous flare(s).

Management of immunosuppressive treatment:

- Baseline glucocorticoids should be kept at <10 mg/day of prednisone equivalent.
- Increasing baseline csDMARDs does not prevent immune toxicity.
- Ongoing trials are evaluating combination of bDMARDs with ICIs.
- Minimal immunosuppressive regimen should be reached in patients with low autoimmune disease activity.
- Selective therapies can be considered as a replacement for non-selective immunosuppressive treatment in patients requiring intensive immunosuppression.

Anticipated monitoring:

- Patients should be educated with regard to symptoms requiring a rapid medical examination.
- Close follow-up should involve autoimmune-disease specialists and oncologists.
- Patients should be referred to a multidisciplinary board for toxicity management if needed.

Tison A, Garaud S, Chiche L, Cornec D, Kostine M. Immune-checkpoint inhibitor use in patients with cancer and pre-existing autoimmune diseases. Nat Rev Rheumatol. 2022;18(11):641-656. doi:10.1038/s41584-022-00841-0

CPI και ΣΕΛ

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Systemic lupus erythematosus reactivation after chemoimmunotherapy in preexisting autoimmune disease

Andrea Spagnoletti, Marco Platania, [...], and Arsela Prelaj +7 View all authors and affiliations

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Abstract

The use of immune checkpoint inhibitors (ICIs) offers new possibilities in modern treatment of many types of cancers. Few data regarding safety and efficacy of ICIs are available, and are mainly from retrospective studies and case reports rather than from clinical trials, in the context of preexisting autoimmune disease, mainly due to the risk of severe toxicity. We present an unexpected life-threatening reactivation of systemic lupus erythematosus after one dose of chemo-immunotherapy with pembrolizumab for oligometastatic non-small-cell lung cancer. We analyze data coming from the published literature in this setting and discuss the risk–benefit balance of immunotherapy in patients with preexisting severe autoimmune disease.

Θεραπεία- Αλλαγή θεραπευτικής στρατηγικής ;

Observational Study > Ann Rheum Dis. 2023 Jul;82(7):920-926. doi: 10.1136/ard-2023-223885. Epub 2023 Apr 5.

Comparative safety and effectiveness of TNF inhibitors, IL6 inhibitors and methotrexate for the treatment of immune checkpoint inhibitor–associated arthritis

Anne R Bass [1 2], Noha Abdel-Wahab [# 3], Pankti D Reid [# 4], Jeffrey A Sparks [# 5], Cassandra Calabrese [# 6], Deanna P Jannat-Khah [7 8], Nilasha Ghosh [9 2], Divya Rajesh [10], Carlos Andres Aude [7], Lydia Gedmintas [11], Lindsey MacFarlane [11], Senada Arabelovic [11], Adewunmi Falohun [3], Komal Mushtaq [12], Farah Al Haj [13], Adi Diab [14], Ami A Shah [15], Clifton O Bingham [16], Karmela Kim Chan [9 2], Laura C Cappelli [16]

Affiliations + expand

PMID: 37019614 DOI: 10.1136/ard-2023-223885

Chatzidionysiou, Katerina et al. “Treatment of rheumatic immune-related adverse events due to cancer immunotherapy with immune checkpoint inhibitors-is it time for a paradigm shift?.” *Clinical rheumatology* vol. 40,5 (2021): 1687-1695. doi:10.1007/s10067-020-05420-w

Bass, Anne R et al. “Comparative safety and effectiveness of TNF inhibitors, IL6 inhibitors and methotrexate for the treatment of immune checkpoint inhibitor-associated arthritis.” Annals of the rheumatic diseases vol. 82,7 (2023): 920-926. doi:10.1136/ard-2023-223885

Take home messages

- Αρθρίτιδα → συχνή ΑΕ
- Συχνότερα συμμετρική οροαρνητική πολυαρθρίτιδα
- Έγκαιρη παραπομπή σε ρευματολόγο→ αύξηση επιβίωσης φαρμάκου +ασθενούς
- Θεραπευτική ομάδα → Ογκολόγος+Ρευματολόγος+Ασθενής
- Θεραπευτικά
  - (1) τοπικά / συστηματικά χορηγούμενα γλυκοκορτικοειδή (μείωση δόσης στην ελάχιστα αποτελεσματική)
  - (2) csDMARDs στις περιπτώσεις ανεπαρκούς απόκρισης σε γλυκοκορτικοειδή ή ως θεραπεία μείωσης δόσης κορτιζόνης (steroi sparing)
  - (3) βιολογικοί παράγοντες (anti-TNF, anti-IL-6)σε σοβαρές ή ανθεκτικές περιπτώσεις
- Προυπάρχον ρευματικό νόσημα- αντένδειξη;


3ο
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ΓΙΑ ΤΗ ΜΥΟΣΚΕΛΕΤΙΚΗ ΥΓΕΙΑ

ΕΥΧΑΡΙΣΤΩ