ΕΠΙΣΤΗΜΟΝΙΚΗ ΕΤΑΙΡΕΙΑ
ΓΙΑ ΤΗ ΜΥΟΣΚΕΛΕΤΙΚΗ ΥΓΕΙΑ

Σε συνεργασία με την
Επιστημονική Ρευματολογική Εταιρεία Κύπρου
Scientific Rheumatology Association of Cyprus

16° ΠΑΝΕΛΛΗΝΙΟ ΣΥΝΕΔΡΙΟ ΕΠΕΜΥ
με διεθνή συμμετοχή

SCIENTIFIC CONFERENCE
ON THE MUSCULOSKELETAL HEALTH

3-6 ΟΚΤΩΒΡΙΟΥ 2024 Ξενοδοχείο Du Lac, ΙΩΑΝΝΙΝΑ

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CONGRESS

ΑΝΤΙΜΕΤΩΠΙΣΗ ΚΑΡΚΙΝΟΠΑΘΩΝ ΜΕ ΠΑΡΑΛΛΗΛΕΣ ΦΛΕΓΜΟΝΩΔΕΙΣ ΝΟΣΟΥΣ

Πως θεραπεύω τον ασθενή με καρκίνο στον οποίο προϋπάρχει ή πρωτοεμφανίζεται Ρευματική Νόσος;

Ευάγγελος Θεοδώρου

Ρευματολόγος

Επιμελητής Ρευματολογικής Κλινικής, 251 Γενικό Νοσοκομείο Αεροπορίας

Σύγκρουση συμφερόντων

- **Καμία για τη συγκεκριμένη παρουσίαση**

Έχω λάβει αμοιβή για ομιλίες και συμβουλευτικές δραστηριότητες (την τελευταία 2ετία) από:

- Novartis, Amgen, Pfizer, Abbvie, Genesis, Aenorasis, GSK, UCB, Pharmaserve-Lilly, SOBI, MSD, FARAN

Γιατί αυτή η παρουσίαση

Βελτίωση της επιβίωσης των ασθενών με νεοπλασίες

- Βελτίωση ΧΜΘ και ΑΚΤΘ
- Εισαγωγή της Ανοσοθεραπείας

Οι ασθενείς με ρευματικά νοσήματα:

- Εμφανίζουν αυξημένες πιθανότητες να εμφανίσουν νεοπλασίες
- Λαμβάνουν θεραπευτικές παρεμβάσεις που πιθανά αυξάνουν την πιθανότητα για νεοπλασίες

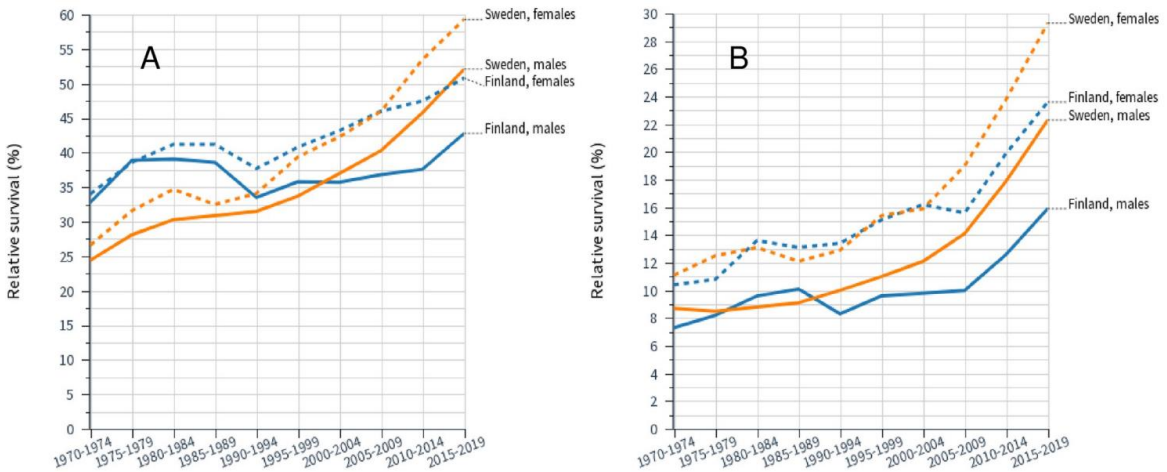
Ασθενείς με νεοπλασίες συχνά εμφανίζουν ρευματικές παθήσεις

- Παρανεοπλασματικά φαινόμενα (Μυοσίτιδες, Ρευματική πολυμυαλγία)
- Ανεπιθύμητες ενέργειες ανοσοθεραπείας

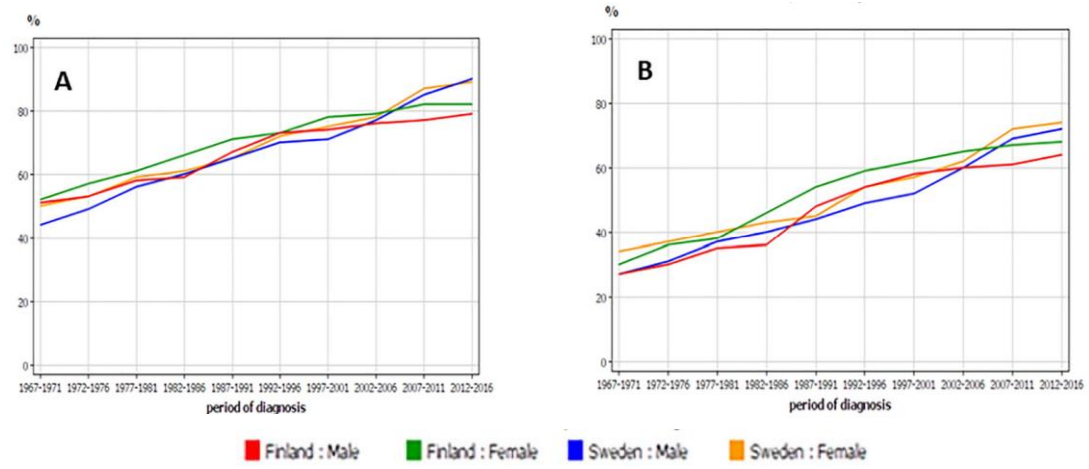
Βελτίωση της επιβίωσης των ασθενών με νεοπλασία

- Πρώιμη διάγνωση
- Αναγνώριση αιτίας (πχ κάπνισμα)
- Επιθετική πρώιμη θεραπεία
- Καλύτερο performance status των ασθενών

Νεοπλασία πνεύμονα



Νεοπλασία νεφρού



1. Hemminki K, Forsti A, Hemminki A, Ljungberg B, Hemminki O (2021) Progress in survival in renal cell carcinoma through 50 years evaluated in Finland and Sweden. PLoS ONE 16(6): e0253236
2. Koskinen A, Hemminki O, Försti A, Hemminki K (2022) Incidence and survival in laryngeal and lung cancers in Finland and Sweden through

Χρόνιες φλεγμονώδεις παθήσεις αυξάνουν τον κίνδυνο για νεοπλασία

J Chron Dis 1978, Vol. 31, pp. 691–696.
© Pergamon Press Ltd. Printed in Great Britain
0021-9681/78/1101-0691$02.00/0

EXCESS RISK OF LYMPHOMAS, LEUKEMIA AND MYELOMA IN PATIENTS WITH RHEUMATOID ARTHRITIS

H. A. ISOMÄKI
Rheumatism Foundation Hospital, 18120 Heinola 12, Finland

T. HAKULINEN
Finnish Cancer Registry, 00170 Helsinki 17, Finland
and
U. JOUTSENLAHTI
Social Insurance Institution of Finland, 00250 Helsinki 25, Finland

(Received in revised form 19 April 1978)

Abstract—The incidence of malignant neoplasms among 11,483 male and 34,618 female individuals with rheumatoid arthritis was studied using two separate nationwide data registers covering the whole Finnish population: the Social Insurance Institution's Population Data Register, which includes information on medication for certain chronic diseases, and the Finnish Cancer Registry, with data on all cancer patients diagnosed in Finland. The follow-up comprised a total of 213,911 person-years.

The total incidence of all malignant neoplasms was higher in males and on the level expected in females. The expected number of cases of leukemia, lymphomas, Hodgkin's disease and myeloma in both sexes was 59.6 as compared with the 130 cases observed. This difference is statistically highly significant ($P < 0.001$). The incidence of cancer of the respiratory organs was higher in males, and the incidence of cancer of the rectum and stomach lower than expected in rheumatoid females

frontiers | Frontiers in Immunology

TYPE Mini Review
PUBLISHED 28 February 2023
DOI 10.3389/fimmu.2023.1095526

Risk of Malignancy in Spondyloarthritis

A Systematic Review

Paras Karmacharya, MBBS[a], Ravi Shahukhal, MD[b], Alexis Ogdie, MD, MSCE[c,*]

KEYWORDS

• Spondyloarthritis • Psoriatic arthritis • Ankylosing spondylitis • Malignancy • Cancer • Tumor necrosis factor inhibitors

KEY POINTS

- There is conflicting evidence on the association between spondyloarthritis (SpA) and malignancies overall.
- There seems to be a higher incidence of nonmelanoma skin cancer in psoriatic arthritis (PsA) and both monoclonal gammopathy of unknown significance and multiple myeloma in ankylosing spondylitis (AS).
- A few studies have reported a higher incidence of lymphoma in both PsA and AS but the results were inconsistent.
- It is unclear if traditional immunosuppressive agents, tumor necrosis factor inhibitors, or nonsteroidal anti-inflammatory drugs modulate the risk of cancer in SpA. However, if there is an increased risk, it seems to be quite small.
- Although no specific screening recommendations for malignancy in SpA are available at present, it would be prudent to perform age-appropriate screening in all patients at minimum with a consideration for annual skin checks in patients with moderate-to-severe psoriasis.

States

Spain

Malignancies in systemic rheumatic diseases: A mini review

Zhe Geng[1†], Cong Ye[2†] and Xiaojian Zhu[3*]

[1]Department of Hematology, Central Hospital of Wuhan, Wuhan, China, [2]Department of Rheumatology and Immunology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [3]Department of Hematology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

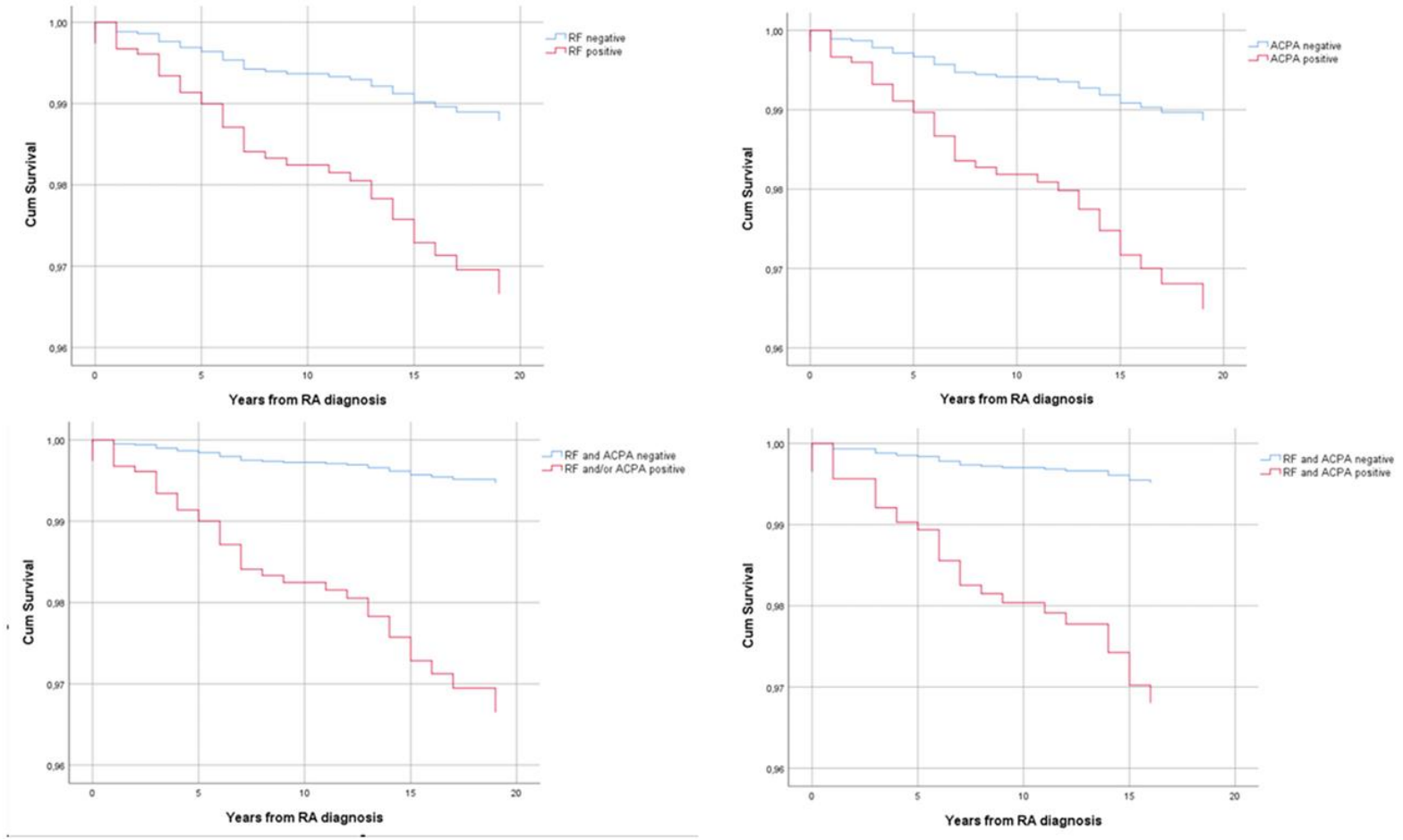
Παράγοντες σε φλεγμονώδεις παθήσεις αυξάνουν τον κίνδυνο για νεοπλασία ;

WHAT THIS STUDY ADDS ⇒

Our study showed that ***RA seropositivity***, in particular anticitrullinated peptide antibody (ACPA) positivity and double seropositivity (rheumatoid factor and ACPA), is a strong and at least seemingly independent risk factor for lung cancer in RA. ***The magnitude of increased risk is 2–6 times, while the absolute risk at 20 years after diagnosis is almost 3%, overall, and over 4% for patients who were ever smokers and had at least one autoantibody.***

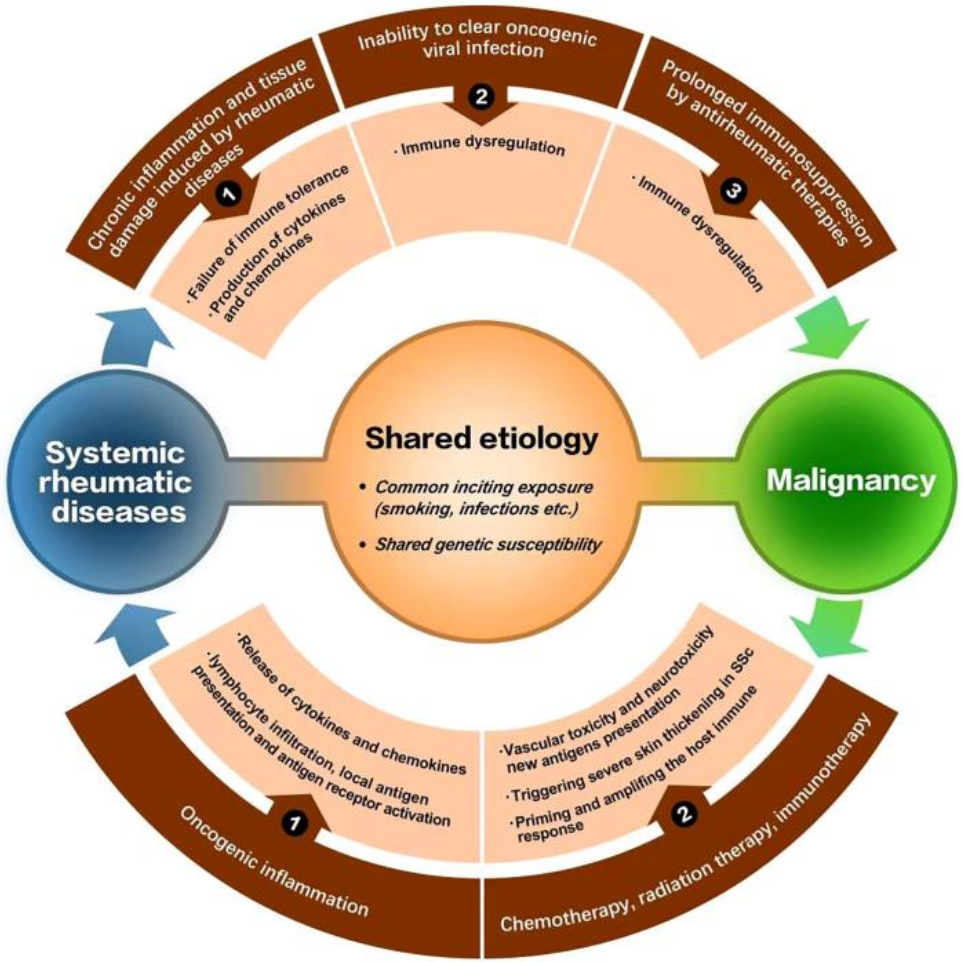
HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY ⇒

Our results raise the question of whether ***regular CT lung screening*** of ever smokers who have autoantibody- positive RA, should be considered



Chatzidionysiou K, di Giuseppe D, Soderling J, et al. Risk of lung cancer in rheu
arthritis and in relation to autoantibody positivity and smoking. RMD Open
2022;8:e002465

Η ανοσοκαταστολή (φυσική ή φαρμακευτική) αυξάνει τον κίνδυνο για νεοπλασία



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

MEDICAL PROGRESS

Skin Cancers after Organ Transplantation

Sylvie Euvrard, M.D., Jean Kanitakis, M.D., and Alain Claudy, M.D.

- 50% των ασθενών λευκής φυλής που υποβλήθηκαν σε μεταμόσχευση συμπαγούς οργάνου και βρίσκονται σε ανοσοκαταστολή θα αναπτύξουν νεοπλασία δέρματος
- 7% το 1ο έτος ως 82% το 10ο έτος
- SIR x 7 σε σχεση με γενικό πληθυσμό

Geng Z, Ye C and Zhu X (2023). Front. Immunol. 14:1095526

Euvrard et al. N Engl J Med. 2003;348(17):1681-91

Μελέτες παρατήρησης και φαρμακοεπαγρύπνηση …

ARTHRITIS & RHEUMATISM
Vol. 46, No. 12, December 2002, pp 3151–3158
DOI 10.1002/art.10679
© 2002, American College of Rheumatology

Tumor Necrosis Factor Antagonist Therapy and Lymphoma Development

Twenty-Six Cases Reported to the Food and Drug Administration

S. Lori Brown,[1] Mark H. Greene,[2] Sharon K. Gershon,[1] Evelyne T. Edwards,[1] and M. Miles Braun[1]

Objective. Etanercept and infliximab are tumor necrosis factor (TNF) antagonists that have been recently approved for the treatment of rheumatoid arthritis (RA) and Crohn's disease (CD). This study was undertaken to investigate the occurrence of lymphoproliferative disorders in patients treated with these agents.

Methods. Relevant data in the MedWatch postmarket adverse event surveillance system run by the US such as this cannot establish a clear causal relationship between exposure to these medications and the risk of lymphoproliferative disease, the known predisposition of patients with RA and CD to lymphoma, the known excess of lymphoma in other immunosuppressed populations, and the known immunosuppressive effects of the anti-TNF drugs provide a biologic basis for concern and justification for the initiation of additional epide-

Rapid onset of cutaneous squamous cell carcinoma in patients with rheumatoid arthritis after starting tumor necrosis factor α receptor IgG1-Fc fusion complex therapy

Kathleen J. Smith, MD,[a] and Henry G. Skelton, MD[b]
Bethesda, Maryland, and Herndon, Virginia

Tumor necrosis factor α (TNF-α) is now believed to be a major contributor to the pathogenesis of the synovitis and joint destruction in rheumatoid arthritis. Etanercept is a recombinant human TNF-α receptor Fc fusion protein consisting of a dimer of the extracellular portion of two p75 TNF-α receptors fused to the Fc portion of human IgG1. Etanercept produces significant dose-dependent improvements in disease activity. We describe 7 patients who experienced 1 or more squamous cell carcinomas that showed rapid growth and arose over a 2- to 4-month period of etanercept therapy. Soluble TNF-α receptor therapy through inhibition of a T_H1 cytokine pattern and inhibition of the direct and indirect cytotoxic effects of TNF-α may initially decrease mechanisms for controlling subclinical tumors and may contribute to the histologic features seen within these tumors. However, prolonged TNF-α inhibition may have some antitumor effects. (J Am Acad Dermatol 2001;45:953-6.)

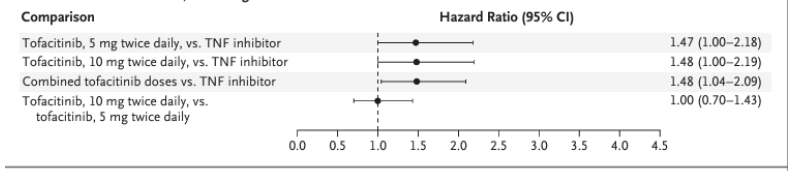
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

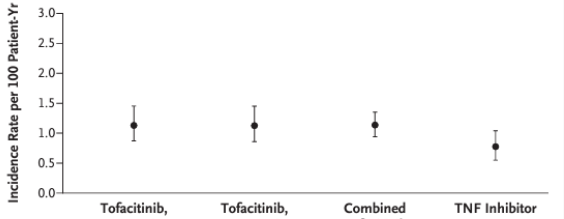
Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis

Steven R. Ytterberg, M.D., Deepak L. Bhatt, M.D., M.P.H., Ted R. Mikuls, M.D., M.S.P.H., Gary G. Koch, Ph.D., Roy Fleischmann, M.D., Jose L. Rivas, M.D., Rebecca Germino, Ph.D., Sujatha Menon, Ph.D., Yanhui Sun, Ph.D., Cunshan Wang, Ph.D., Andrea B. Shapiro, M.D., Keith S. Kanik, M.D., and Carol A. Connell, R.N., Ph.D., for the ORAL Surveillance Investigators*

A Hazard Ratio for Cancers, Excluding NMSC



B Incidence Rate for Cancers, Excluding NMSC



No. of Patients with First Event/Total No. (%)	62/1455 (4.3)	60/1456 (4.1)	122/2911 (4.2)	42/1451 (2.9)
No. of Patient-Yr	5491.48	5311.71	10,803.19	5482.30
Incidence Rate per 100 Patient-Yr (95% CI)	1.13 (0.87–1.45)	1.13 (0.86–1.45)	1.13 (0.94–1.35)	0.77 (0.55–1.04)
NNH (patient-yr) vs. TNF Inhibitor	276	275	—	—
NNH (over 5-yr period) vs. TNF Inhibitor	55	55	—	—

Patient medication guides & Black box warnings …

MEDICATION GUIDE
DRUG-X (pronunciation spelling)
(drugimab-cznm)
injection, for intramuscular use

What is the most important information I should know about DRUG-X?
…

What is DRUG-X?
…

Who should not take DRUG-X?
…

Before taking DRUG-X, tell your healthcare provider about all of your medical conditions, including if you:
…

How should I take DRUG-X?
…

What should I avoid while taking DRUG-X?
…

What are the possible side effects of DRUG-X?
…
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store DRUG-X?
…

General information about the safe and effective use of DRUG-X.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use DRUG-X for a condition for which it was not prescribed. Do not give DRUG-X to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about DRUG-X that is written for health professionals.

What are the ingredients in DRUG-X?
Active ingredients:
Inactive ingredients:

Manufactured for:
Manufactured by:

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: MM/YYYY

Based on current knowledge, a possible risk for the development of lymphomas, leukaemia or other haematopoietic or solid malignancies in patients treated with a TNF-antagonist cannot be excluded. ***Caution*** *should be exercised when considering TNF-antagonist therapy for patients with a history of malignancy or when considering continuing treatment in patients who develop a malignancy.*

No studies have been conducted that include patients with a history of malignancy or in whom treatment with (a TNF-antagonist) is continued following development of malignancy. Thus, additional ***caution*** *should be exercised in considering (TNF-antagonist) treatment of these patients*

Consider the risks *and benefits of TNF-blocker treatment … prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing a TNF blocker in patients who develop a malignancy*

FDA Search Menu

IN THIS SECTION

← Drug Safety and Availability

FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions

Approved uses also being limited to certain patients

Επιφύλαξη για προωθημένη θεραπεία σε ασθενείς με νεοπλασία

Rheumatoid arthritis

RMD Open
Rheumatic & Musculoskeletal Diseases

Short report

How do we use biologics in rheumatoid arthritis patients with a history of malignancy? An assessment of treatment patterns using Scandinavian registers

Katerina Chatzidionysiou,[1] Bénédicte Delcoigne,[1] Thomas Frisell,[1] Merete L Hetland,[2,3] Bente Glintborg,[2,3] Iene dreyer,[4,5] René Cordtz,[6] Kristian Zobbe,[6] Dan Nordström,[7] Nina Trokovic,[7] Kalle Aaltonen,[8] Sella Aarrestad Provan,[9] Gerdur Grondal,[10] Bjorn Gudbjornsson,[11] Johan Askling[1]

1. ***Most treatment guidelines have therefore issued caution against using bDMARDs*** (tumour necrosis factor inhibitors (TNFi) in particular) in patients with a history of cancer within 5–10 years.
2. So far, most (though not all) studies of cancer incidence following treatment with TNFi and other bDMARDs, and of ***recurrence of pretreatment cancers following treatment with TNFi, have been reassuring***
3. The 2015 ACR recommendations for treatment of rheumatoid arthritis (RA) recommend that ***patients with a history of previous solid organ malignancy should be treated as patients without this condition***, though acknowledging the ***low level of evidence***, whereas previous recommendations suggested rituximab.
4. Similarly, there ***is no consensus regarding the time period from cancer diagnosis until the safe initiation of a bDMARD***

Key messages

What is already known about this subject?

- According to RA treatment recommendations, patients with a history of previous solid organ malignancy should be treated as patients without this condition, although the level of evidence is low.

What does this study add?

- This large multinational register-based study quantified the proportion of RA patients starting a bDMARD who had a prior malignancy (1–6%). This proportion was significantly higher for rituximab (8–17%), demonstrating a preference for rituximab in this patient population.

How might this impact on clinical practice?

- There is a reluctancy to use bDMARDs and especially TNF inhibitors in RA patients with a history of malignancy, which might imply a risk for undertreatment of some patients. This underscores the need for more data.

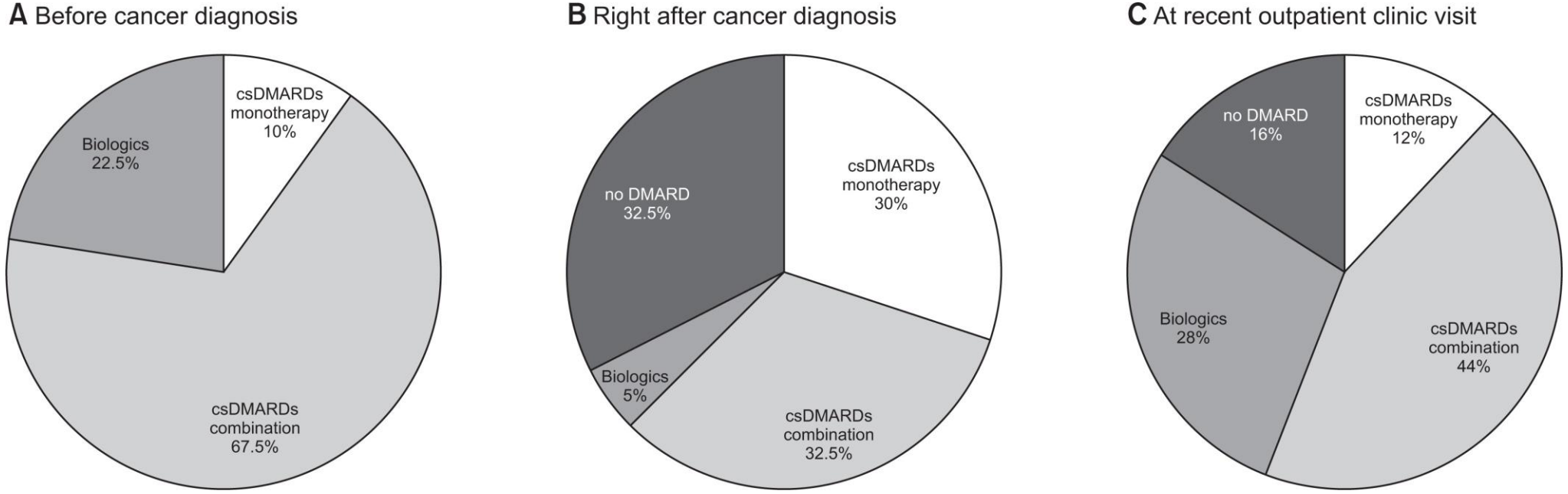
Chatzidionysiou K, Delcoigne B, Frisell T, et al. How do we use biologics in rheumatoi
arthritis patients with a history of malignancy? An assessment of treatment patterns

...Καθώς περνάει ο χρόνος αυξάνεται η χρήση προωθημένης θεραπεία σε ασθενείς με νεοπλασία

J Rheum Dis 2022;29(3):162-170
https://doi.org/10.4078/jrd.2022.29.3.162
pISSN: 2093-940X, eISSN: 2233-4718
Original Article

Use of Disease-modifying Antirheumatic Drugs After Cancer Diagnosis in Rheumatoid Arthritis Patients

Young Bin Joo, M.D.[1], Seung Min Jung, M.D.[2], Yune-Jung Park, M.D.[2], Ki-Jo Kim, M.D.[2], Kyung-Su Park, M.D.[2]



J Rheum Dis

Υπάρχουν ισχυρές αποδείξεις;

Διπλά τυχαιοποιημένες μελέτες (RCTs)

- …Ανήθικο
- Στις RCTs των αντιρευματικών φαρμάκων εξαιρούνται οι ασθενείς με νεοπλασίες
- Μικρό χρονικό διάστημα παρακολούθησης (ακόμα και open label)
- Μικρός αριθμός συμμετεχόντων

Μητρώα ασθενών με πραγματικά δεδομένα (Registries-RWE):

- Μεγάλος αριθμός ασθενών
- Παρακολούθηση για πολλά έτη
- Λαμβάνουν και άλλες θεραπευτικές παρεμβάσεις που πιθανά αυξάνουν την πιθανότητα για νεοπλασίες
- Ετερόκλητος πληθυσμός

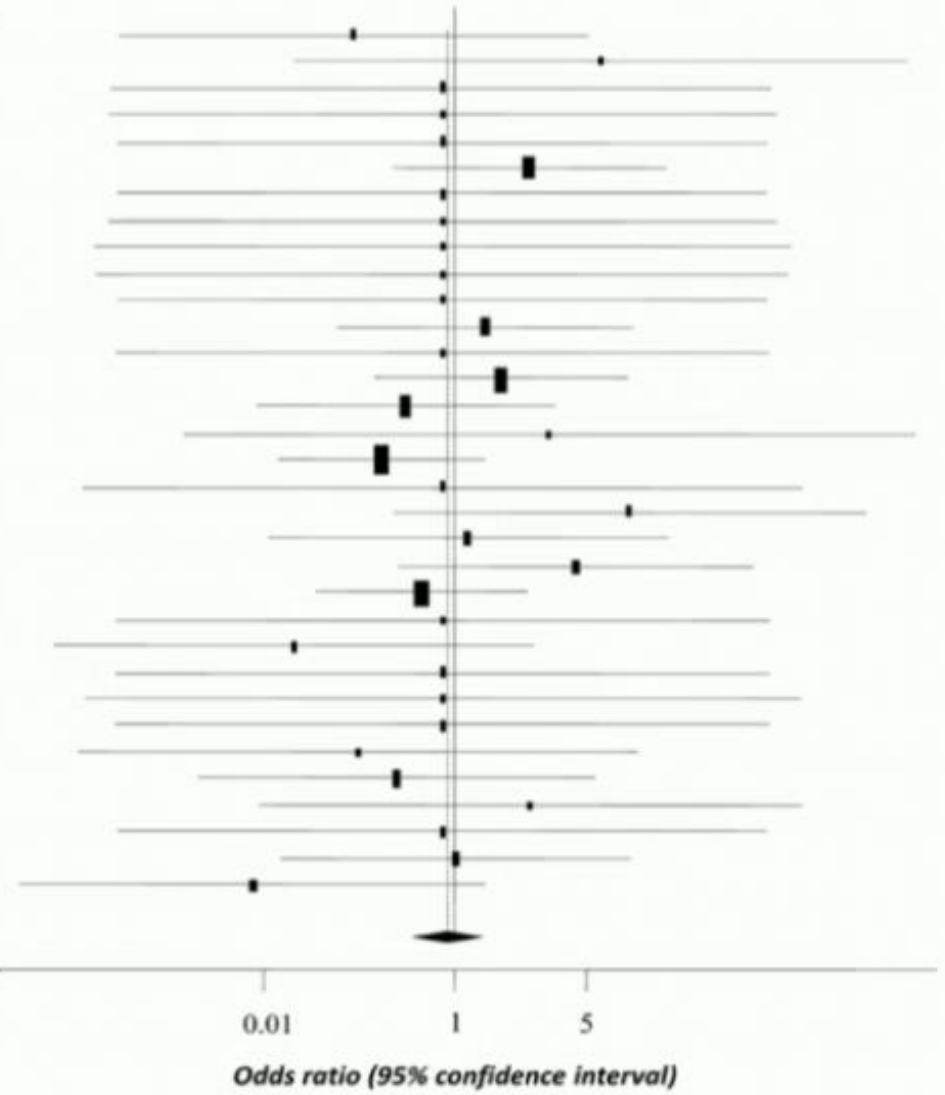
Basic / Translational science

- Εργαστήριο vs πραγματική ζωή
- Έλλειψη «συνολικής» παθοφυσιολογίας (μοντέλα νόσων)

RCTs: Ασθενείς υπό αγωγή με TNFi ± csDMARDs και εμφάνιση νεοπλασίας

Trial	Anti-TNF-α	Number of cancers/number of patients		Weight (%)	Odds ratio [95% CI]
		Anti-TNF-α arm	Placebo arm		
Maini, 2004	IFX	1/48	0/15	2.44	0.30 [0.02-5.07]
Saint Clair, 2004	IFX	4/652	0/245	1.42	5.92 [0.15-238.17]
Taylor, 2004	IFX	0/12	0/11	1.22	0.87 [0.02-48.04]
Quinn, 2005	IFX	0/9	0/10	1.17	0.87 [0.02-50.19]
Abe, 2006	IFX	0/48	0/42	1.27	0.88 [0.02-45.12]
Westhovens, 2006	IFX	5/306	2/303	7.20	2.50 [0.48-12.99]
Leirisalo-Repo, 2009	IFX	0/46	0/45	1.27	0.88 [0.02-45.37]
Moreland, 1997	ETN	0/41	0/23	1.17	0.88 [0.02-50.28]
Weinblatt, 1999	ETN	0/57	0/24	1.12	0.88 [0.01-59.22]
Moreland, 1999	ETN	0/59	0/26	1.12	0.88 [0.01-57.24]
Ericson, 1999	ETN	0/105	0/85	1.27	0.88 [0.02-44.77]
Bathon, 2000	ETN	3/179	2/174	5.99	1.47 [0.24-8.88]
Lan, 2004	ETN	0/27	0/27	1.22	0.87 [0.02-46.13]
van der Heijde, 2006	ETN	9/311	2/121	8.17	1.77 [0.38-8.33]
Weisman, 2007	ETN	2/231	3/197	6.04	0.56 [0.09-3.41]
Combe, 2009	ETN	2/67	0/16	1.01	3.20 [0.04-268.77]
Emery, 2010	ETN	4/108	7/83	12.23	0.42 [0.12-1.48]
Weinblatt, 2003	ADA	0/50	0/18	1.01	0.88 [0.01-67.74]
Furst, 2003	ADA	4/294	0/288	2.38	8.42 [0.48-146.61]
van de Putte, 2004	ADA	2/83	1/49	3.30	1.19 [0.10-13.42]
Keystone, 2004	ADA	5/164	1/141	4.16	4.40 [0.51-38.14]
Breedveld , 2006	ADA	6/376	4/173	11.92	0.69 [0.19-2.46]
Kim, 2007	ADA	0/55	0/40	1.27	0.88 [0.02-45.86]
Miyasaka, 2008	ADA	0/59	2/38	2.33	0.14 [0.01-2.64]
Bejarano, 2008	ADA	0/50	0/36	1.22	0.88 [0.02-46.05]
Chen, 2009	ADA	0/32	0/12	1.01	0.87 [0.01-66.48]
Kay, 2008	GMM	0/31	0/29	1.27	0.88 [0.02-45.68]
Keystone, 2009	GMM	0/72	1/85	1.67	0.32 [0.01-9.45]
Emery, 2009	GMM	1/151	2/152	3.35	0.50 [0.04-5.57]
Tanaka, 2010	GMM	1/76	0/38	1.78	2.55 [0.09-68.96]
Takeuchi, 2010	GMM	0/96	0/92	1.27	0.88 [0.02-44.80]
Keystone, 2008	CTZ	7/252	1/37	4.31	1.03 [0.12-8.61]
Smolen, 2009	CTZ	1/171	1/16	2.44	0.09 [0.01-1.48]
Combined	**All**	**57/4318**	**30/2711**	**100**	**0.93 [0.59-1.44]**

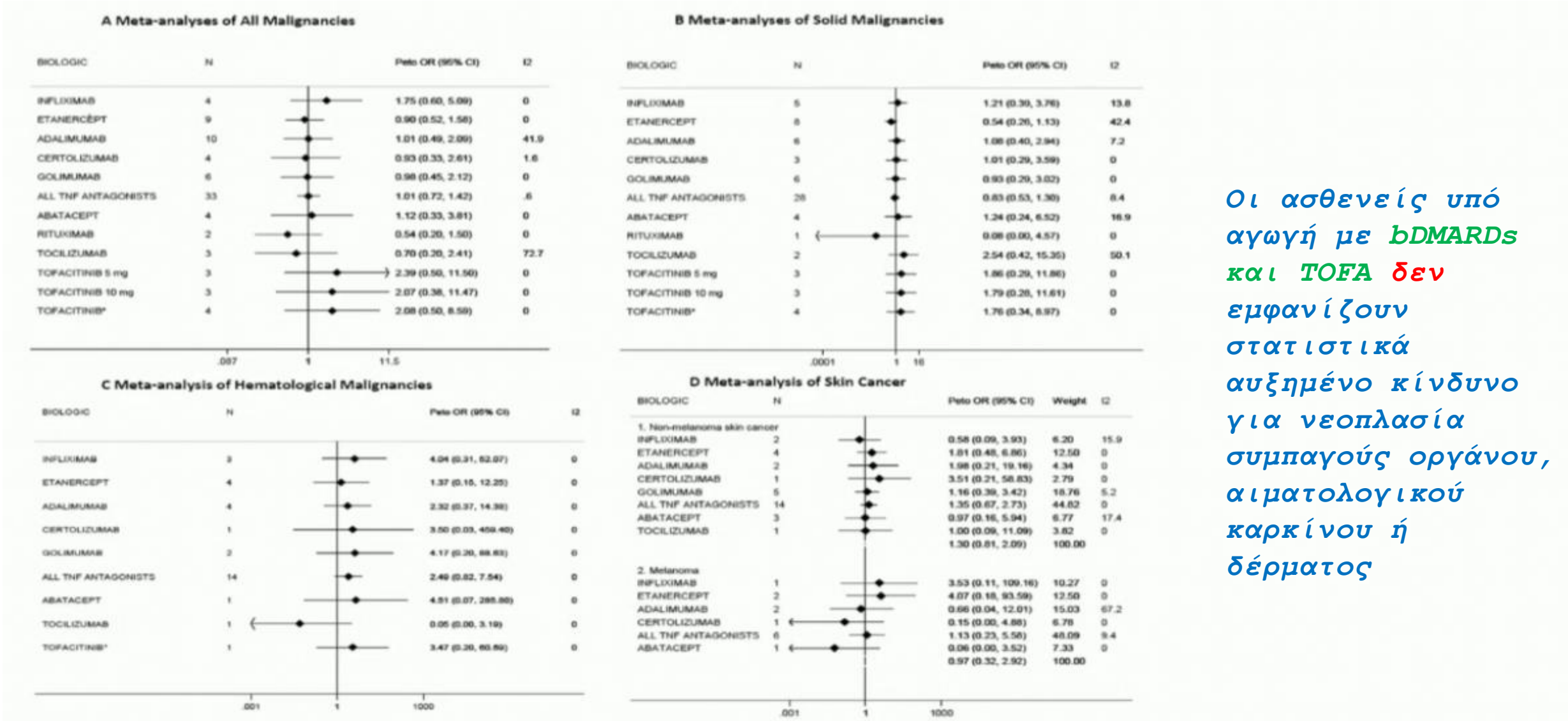
Test for overall effect: p=0.73
Heterogeneity: Cochran's Q=15.83 I^2=0%
Publication bias (Egger test): p=0.79



Οι ασθενείς υπό αγωγή με **TNFi** – με ή χωρίς συγχορήγηση csDMARD – δεν εμφανίζουν στατιστικά αυξημένο κίνδυνο για νεοπλασία

Moulis et al. PLoS One. 2012;7(11):e48991.

RCTs: Ασθενείς υπό αγωγή με b-tsDMARDs και εμφάνιση νεοπλασίας (PA)



N: Number of included studies; I2: I^2 (Heterogeneity); Tofacitinib*: all doses of tofacitinib (5 mg BID and 10 mg BID)

Οι ασθενείς υπό αγωγή με bDMARDs και TOFA δεν εμφανίζουν στατιστικά αυξημένο κίνδυνο για νεοπλασία συμπαγούς οργάνου, αιματολογικού καρκίνου ή δέρματος

Maneiroa et al. Seminars in Arthritis and Rheumatism 47 (2017) 149–156

Κίνδυνος σε ασθενείς με PA υπό θεραπεία σε σχέση με γενικό πληθυσμό

RHEUMATOLOGY

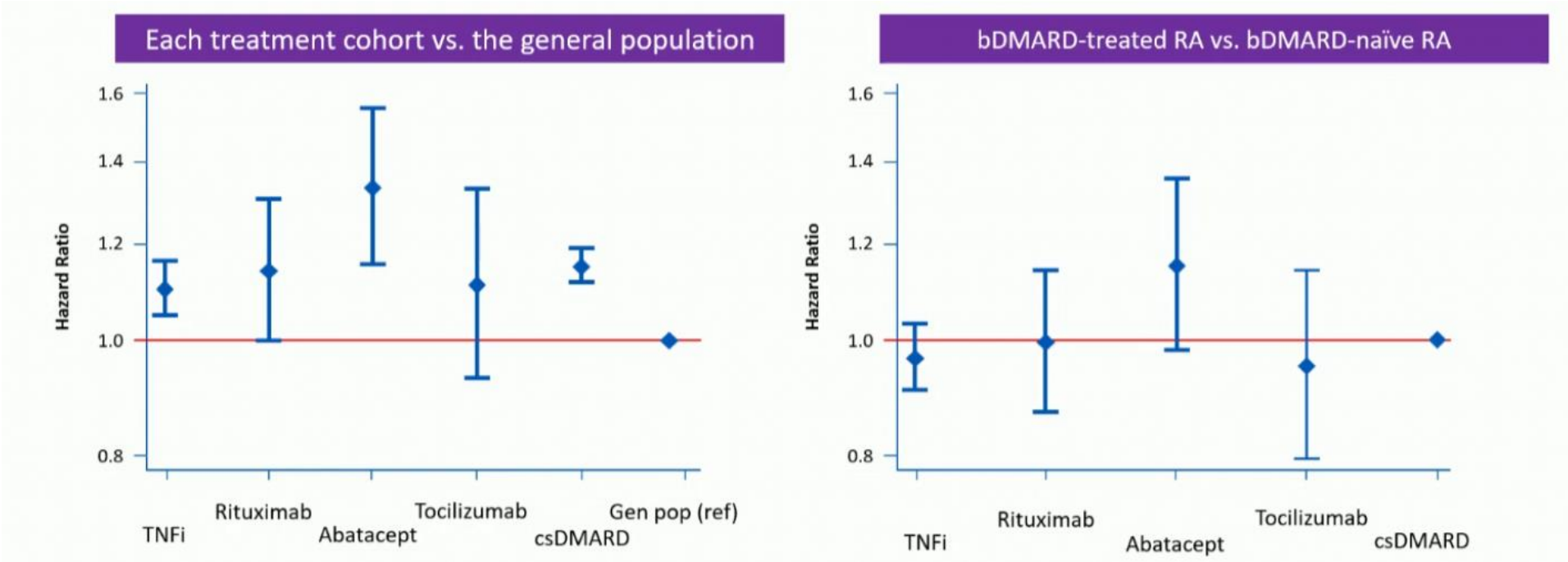
Rheumatology 2022;61:1810–1818
doi:10.1093/rheumatology/keab570
Advance Access publication 29 July 2021

Original article

Short- and longer-term cancer risks with biologic and targeted synthetic disease-modifying antirheumatic drugs as used against rheumatoid arthritis in clinical practice

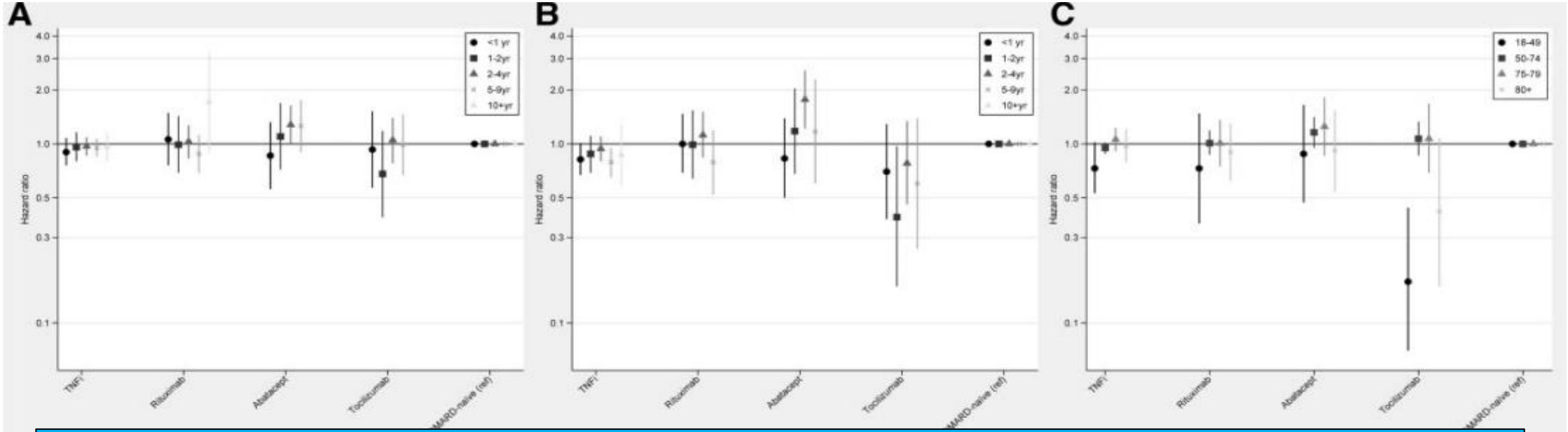
Viking Huss [1,2], Hannah Bower[1], Hjalmar Wadström [1], Thomas Frisell[1] and Johan Askling[1,2]; on behalf of the ARTIS group*

Cohort	Patient episodes	Events	Person-years of follow-up	Crude incidence per 1000	HRa (95% CI) B/tsDMARD-naïve	HRb (95% CI)	HRa (95% CI) general population
TNFi	33 609	2395	224 661.2	10.7	1.0 (0.9, 1.0)	1.0 (0.9, 1.0)	1.1 (1.0, 1.2)[a]
RTX	4367	294	22 846.9	12.9	1.0 (0.9, 1.1)	1.0 (0.9, 1.1)	1.1 (1.0, 1.3)[b]
ABT	3558	180	13 604.6	13.6	1.2 (1.0, 1.4)[c]	1.2 (1.0, 1.3)[d]	1.3 (1.1, 1.6)
TCZ	2895	119	11 572.3	11.6	1.0 (0.8, 1.2)	1.0 (0.8, 1.2)	1.1 (0.9, 1.3)
B/tsDMARD-naïve	58 233	5642	38 5173.5	14.6	1.0 (reference)	1.0 (reference)	1.2 (1.1, 1.2)[e]
General population	215 592	13 205	1 335 994.4	9.9	0.9 (0.8, 0.9)	NA	1.0 (reference)



Huss V. et al.Rheumatology 2022;61:1810-1818

Κίνδυνος σε ασθενείς με PA υπό θεραπεία σε σχέση με τον γενικό πληθυσμό



(A)Χρονική έναρξη θεραπείας (έτη) (B) Χρονική διαρκεια θεραπείας

Rheumatology key messages

- We found no increased risk for cancer overall in RA patients treated with TNFis, anti-CD20 or anti-IL6.
- For RA patients treated with abatacept, we noted a potential signal of increased risk for cancer overall.
- A potential signal for increased risk for urinary tract cancer for RA patients treated with TNFis, rituximab, abatacept and tocilizumab was identified.

Huss V. et al.Rheumatology 2022;61:1810-1818

EXTENDED REPORT

Risk of second malignant neoplasm and mortality in patients with rheumatoid arthritis treated with biological DMARDs: a Danish population-based cohort study

Lene Dreyer,[1,2] René L Cordtz,[1,2] Inger Marie J Hansen,[3,4] Lars Erik Kristensen,[2] Merete L Hetland,[5,6,7] Lene Mellemkjaer[8]

Η συχνότητα της εμφάνισης 2η νεοπλασίας δεν αλλάζει με ή χωρίς τη χορήγηση bDMARDs

Table 2 Observed numbers (Obs) and HRs of a SMN in patients with rheumatoid arthritis according to bDMARD treatment

Treatment	SMN, Obs	Person-years	HR* (95% CI)
Non-use of bDMARDs	70†	2461	1 (Ref)
Ever bDMARDs	38	1225	1.11 (0.74 to 1.67)
bDMARDs before first cancer	11‡	272	1.06 (0.52 to 2.14)
bDMARDs after first cancer	27	953	1.13 (0.71 to 1.80)
bDMARDs only after first cancer	21§	760	1.15 (0.68 to 1.95)
bDMARDs both before and after first cancer	6¶	193	1.09 (0.46 to 2.57)
Type of bDMARD after first cancer**			
TNF-I	21	723	1.21 (0.73 to 2.03)
Rituximab	7	235	1.05 (0.47 to 2.34)

r, calendar time and cancer site.

Table 3 Observed number (Obs) of deaths and overall mortality in patients with rheumatoid arthritis with cancer according to bDMARD treatment

	All n=1678			Extent of disease recorded n=1326			
Treatment	Deaths Obs	Person-years	Adjusted* HR (95% CI)	Deaths Obs	Person-years	Adjusted* HR (95% CI)	Further adjusted† HR (95% CI)
Non-user of bDMARDs	207	2461	1 (Ref)	150	2022	1 (Ref)	1 (Ref)
Ever bDMARDs	135	1225	1.25 (0.99 to 1.57)	110	982	1.35 (1.04 to 1.76)	1.23 (0.94 to 1.60)
bDMARDs before first cancer	93	272	1.50 (1.15 to 1.97)	75	214	1.53 (1.13 to 2.09)	1.20 (0.88 to 1.63)
bDMARDs after first cancer	42	953	0.92 (0.64 to 1.31)	35	767	1.08 (0.73 to 1.61)	1.29 (0.86 to 1.94)
bDMARDs only after first cancer	23	760	1.01 (0.62 to 1.65)	20	640	1.19 (0.69 to 2.04)	1.36 (0.78 to 2.39)
bDMARDs both before and after first cancer	19	193	0.85 (0.52 to 1.38)	15	128	0.99 (0.57 to 1.73)	1.22 (0.70 to 2.13)
Type of bDMARD after first cancer‡							
TNF-I	35	723	0.96 (0.66 to 1.41)	29	568	1.13 (0.73 to 1.74)	1.42 (0.91 to 2.20)
Rituximab	9	235	0.86 (0.43 to 1.72)	8	205	1.13 (0.54 to 2.40)	1.11 (0.53 to 2.35)

*Adjusted for age, gender, calendar time, cancer site.

Η θνητότητα δεν αλλάζει σε ποσοστό με τη χρήση ή όχι bDMARDs, είτε λάμβανε πριν είτε μετά τη νεοπλασία την θεραπεία

Dreyer L, Cordtz RL, Hansen IMJ, et al. Ann Rheum Dis 2018;77:510–514.

Ασθενείς υπό αγωγή με bDMARDs vs csDMARDs και υποτροπή της νεοπλασίας

RHEUMATOLOGY

Rheumatology 2020;59:930-939
doi:10.1093/rheumatology/kez475
Advance Access publication 17 October 2019

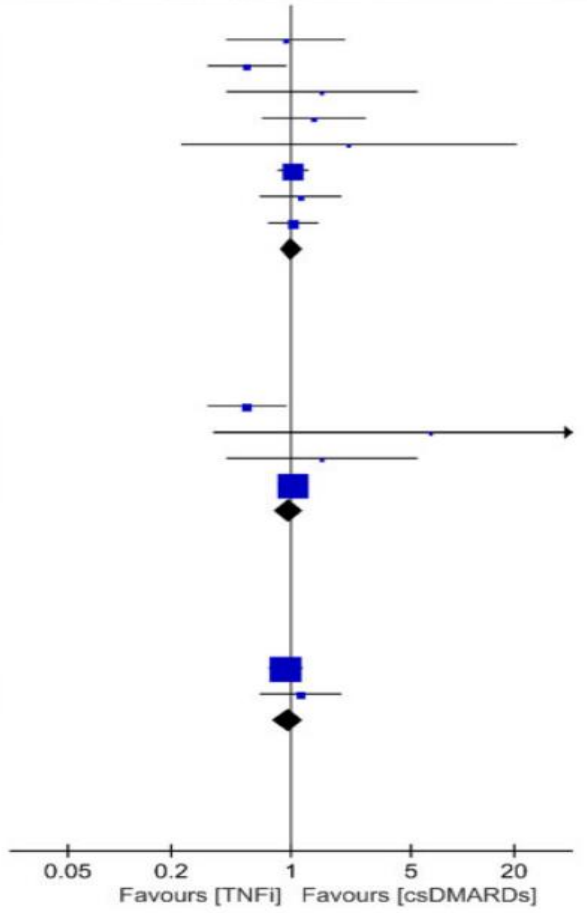
Systematic Review and Meta-analysis

A meta-analysis of biologic therapies on risk of new or recurrent cancer in patients with rheumatoid arthritis and a prior malignancy

Wenhui Xie [1], Shiyu Xiao[2], Yanrong Huang[1], Xiaoying Sun[1], Dai Gao[1], LanLan Ji[1], Guangtao Li[1] and Zhuoli Zhang[1]

Οι ασθενείς με PA υπό αγωγή με TNFi ή RTX δεν εμφανίζουν στατιστικά αυξημένο κίνδυνο για νεοπλασία συμπαγούς οργάνου, δέρματος ή μαστού

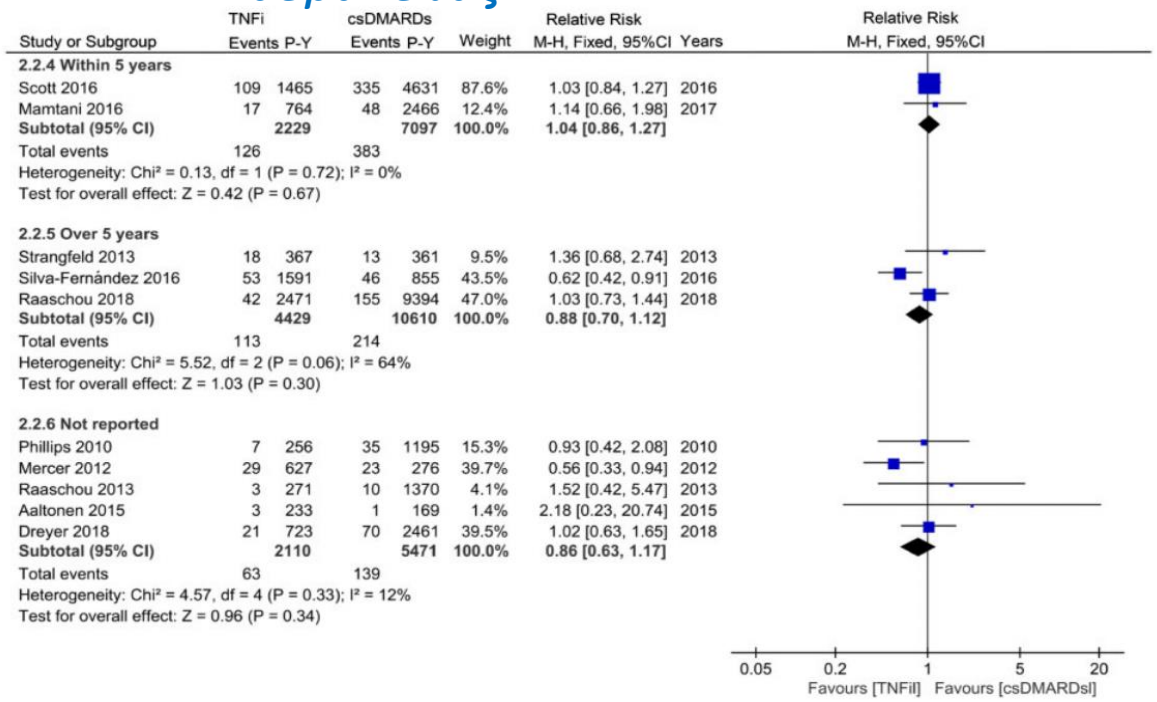
Study or Subgroup	TNFi Events	TNFi P-Y	csDMARDs Events	csDMARDs P-Y	Weight	Relative Risk M-H, Fixed, 95%CI	Years
2.1.1 Solid cancer							
Phillips 2010	7	256	35	1195	4.0%	0.93 [0.42, 2.08]	2010
Mercer 2012	29	627	23	276	10.3%	0.56 [0.33, 0.94]	2012
Raaschou 2013	3	271	10	1370	1.1%	1.52 [0.42, 5.47]	2013
Strangfeld 2013	18	367	13	361	4.2%	1.36 [0.68, 2.74]	2013
Aaltonen 2015	3	233	1	169	0.4%	2.18 [0.23, 20.74]	2015
Scott 2016	109	1465	335	4631	51.9%	1.03 [0.84, 1.27]	2016
Mamtani 2016	17	764	48	2466	7.3%	1.14 [0.66, 1.98]	2017
Raaschou 2018	42	2471	155	9394	20.8%	1.03 [0.73, 1.44]	2018
Subtotal (95% CI)		**6454**		**19862**	**100.0%**	**1.01 [0.87, 1.17]**	
Total events	228		620				
Heterogeneity: Chi² = 6.74, df = 7 (P = 0.46); I² = 0%							
Test for overall effect: Z = 0.11 (P = 0.91)							
2.1.2 Skin cancer							
Mercer 2012	29	627	23	276	16.2%	0.56 [0.33, 0.94]	2012
Strangfeld 2013	3	30	0	28	0.3%	6.55 [0.35, 121.37]	2013
Raaschou 2013	3	271	10	1370	1.7%	1.52 [0.42, 5.47]	2013
Scott 2016	109	1465	335	4631	81.8%	1.03 [0.84, 1.27]	2016
Subtotal (95% CI)		**2393**		**6305**	**100.0%**	**0.97 [0.81, 1.18]**	
Total events	144		368				
Heterogeneity: Chi² = 6.71, df = 3 (P = 0.08); I² = 55%							
Test for overall effect: Z = 0.27 (P = 0.79)							
2.1.3 Breast cancer							
Raaschou 2015	120	592	120	550	84.6%	0.93 [0.74, 1.16]	2015
Mamtani 2016	17	764	48	2466	15.4%	1.14 [0.66, 1.98]	2017
Subtotal (95% CI)		**1356**		**3016**	**100.0%**	**0.96 [0.78, 1.18]**	
Total events	137		168				
Heterogeneity: Chi² = 0.47, df = 1 (P = 0.49); I² = 0%							
Test for overall effect: Z = 0.36 (P = 0.72)							



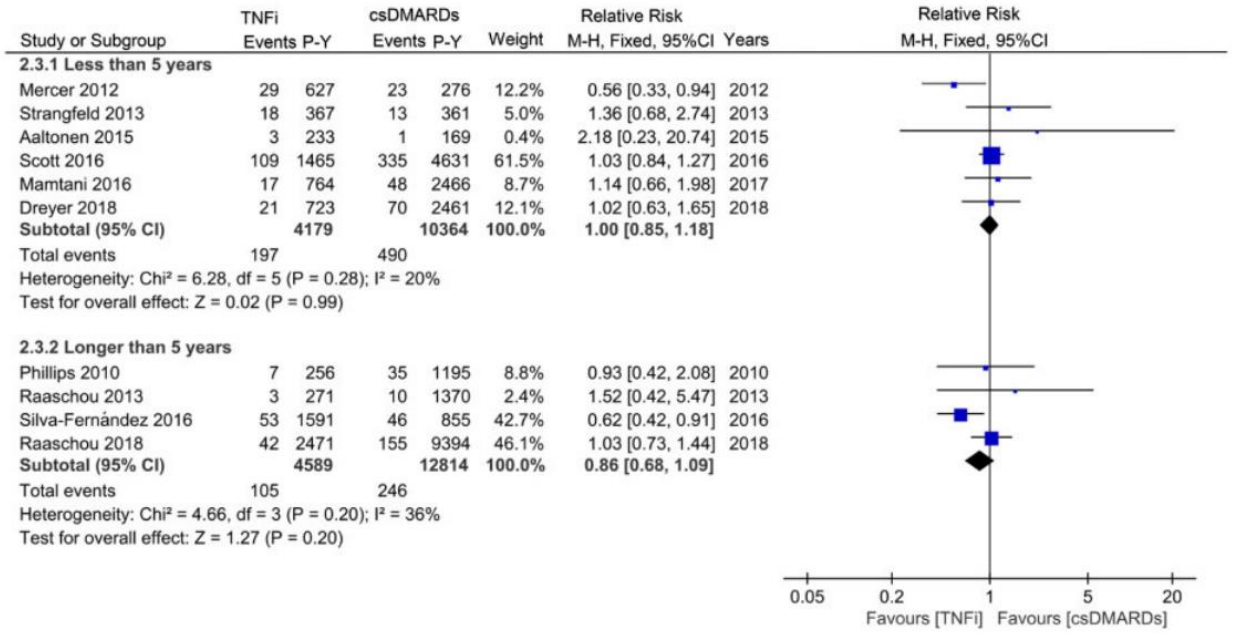
Xie W. et al. Rheumatology (Oxford) 2020 May

Ασθενείς υπό αγωγή με TNFi vs csDMARDs και υποτροπή της νεοπλασίας

Χρόνος έναρξης θεραπείας



Χρόνος έκθεσης στη θεραπεία



Rheumatology key messages

- Risk of cancer recurrence was generally similar between biologics and csDMARDs therapies.
- Stratifying cancer types, interval of TNFi initiation, or TNFi exposure period, founds similar results.
- Rheumatologists could safely administer biologics in RA patients with previous cancer in general.

Xie W. et al. Rheumatology (Oxford) 2020 May

Not a guideline …but a good start!!!

15:45 - 17:00 EULAR Recommendations I

Chairs: Ernest Choy, Kati Mykkänen

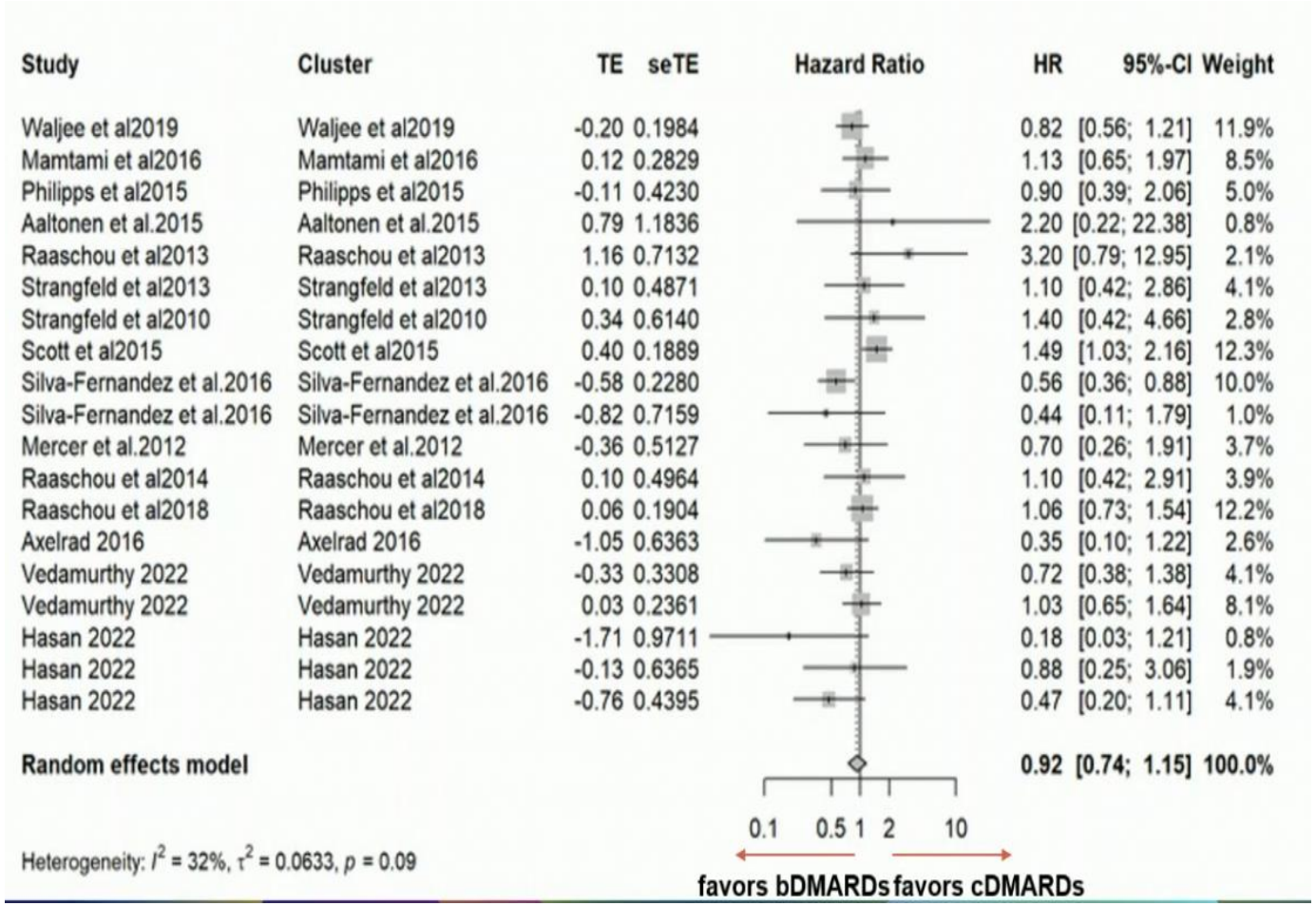
EULAR Points to Consider on the initiation of targeted therapies in patients with inflammatory arthritis and a history of cancer

EULAR Task Force

Jacques-Eric Gottenberg

EULAR Points to Consider on the initiation of targeted therapies in patients with inflammatory arthritide and a history of cancer

Ασθενείς υπό αγωγή με bDMARDs vs csDMARDs και εμφάνιση νέας ή υποτροπή νεοπλασίας



Οι ασθενείς υπό αγωγή με bDMARDs δεν εμφανίζουν στατιστικά αυξημένο κίνδυνο για νεοπλασία συμπαγούς οργάνου, αιματολογικού καρκίνου ή δέρματος

Characteristics of the studies

Type of DMARDs	Number of patients	Number of patient-years
cDMARDs	18000	61713
Anti-TNF	4162	13519
Rituximab	100	261
Vedolizumab	130	1087
Ustekinumab	66	228
Anakinra	9	31

- **4 years** : Median time between cancer diagnosis and TT(bDMARD initiation)
- Mostly concern anti-TNF
- Median follow up after TT initiation : **2.7 years** (9.8 months to 8.8 years).

With such a limited follow-up, results should be interpreted with caution

Sebbag E, Lauper K, Molina Collada J, et al Annals of the Rheumatic Diseases 2023;82:29

Points to consider…

	Overaching principles
A	These PTC are underpinned by the EULAR recommendations for the management of inflammatory arthritis (i.e., RA, SpA)
B	New-onset or recurrent cancer can occur in patients with inflammatory arthritis with a history of cancer
C	Individualized risk of cancer recurrence needs to be assessed based on the characteristics of the patient, the cancer and the underlying inflammatory arthritis
D	The rheumatologist is responsible for the management of patients with inflammatory arthritis and a history of cancer
E	Treatment of patients with inflammatory arthritis and a history of cancer should aim at optimizing outcomes and must be based on a shared decision between the patient and the rheumatologist

	Points to consider
1	Treating inflammatory arthritis effectively in patients with a history of cancer is important to reduce the potential associated risk of malignancy
2	The risk of complications associated with undertreated inflammatory activity should be balanced against the potential risk of targeted antirheumatic therapy-related cancer recurrence.
3	The rheumatologist should engage with other specialists caring for cancer for the co-management of patients with inflammatory arthritis and a history of cancer

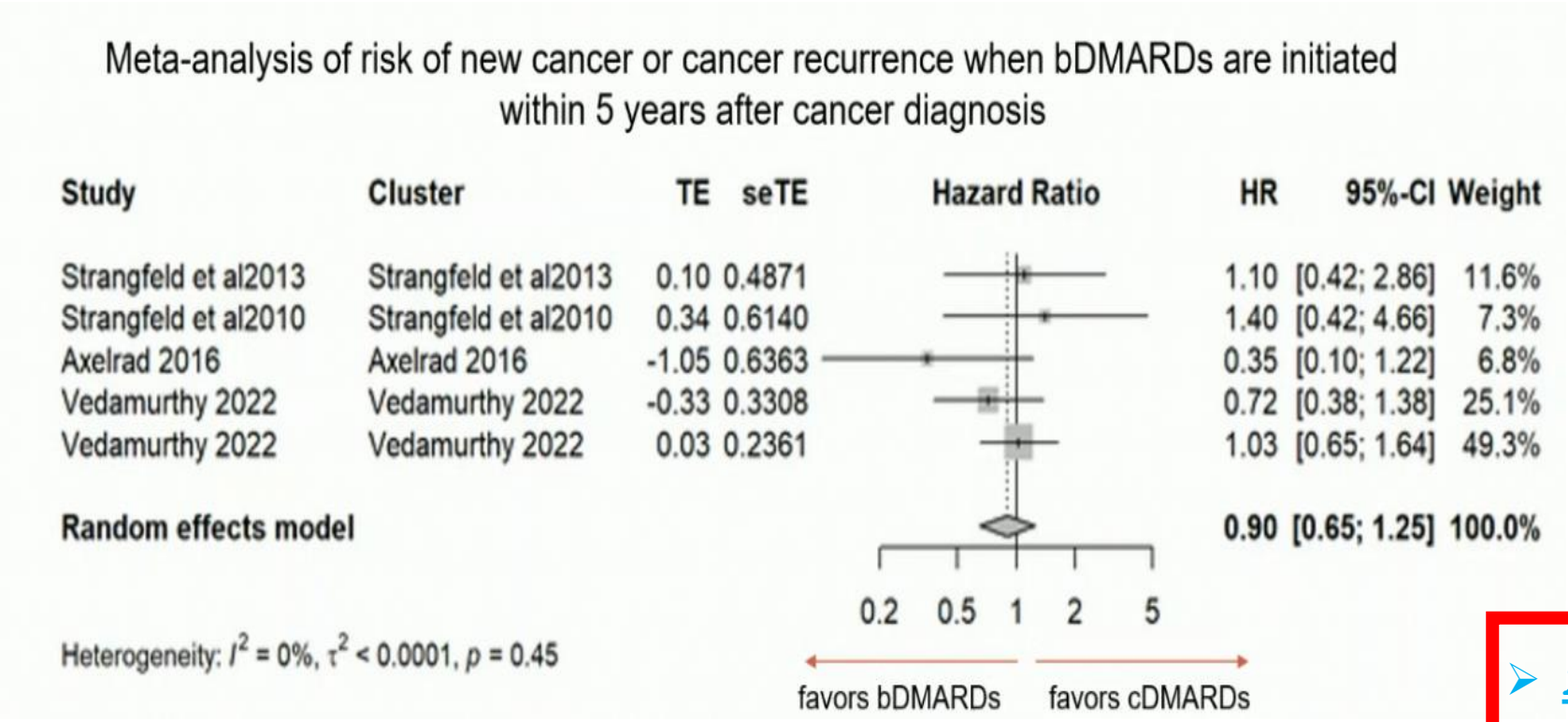
Sebbag E, Lauper K, Molina Collada J, et al Annals of the Rheumatic Diseases 2023;82:29

Πότε πρέπει (ή μπορώ…) να αρχίσω τη θεραπεία σε ασθενή με νεοπλασία και ρευμ. νόσο

PTC 4. Appropriate targeted anti-rheumatic treatment **can be** initiated **without delay** in patients with a cancer in remission

Γνώμη του Ογκολόγου;

Meta-analysis of risk of new cancer or cancer recurrence when bDMARDs are initiated within 5 years after cancer diagnosis



✓ *Ενεργός ρευματική νόσος*

✓ *Στάθμιση κινδύνου* μεταξύ

- *ενεργότητας νόσου*
- *παραγόντων κινδύνου υποτροπής νεοπλασίας*

➢ *Χωρίς περιορισμό στο χρόνο έναρξης*

Sebbag E, Lauper K, Molina Collada J, et al Annals of the Rheumatic Diseases 2023;82:29

Επιφύλαξη σε ορισμένες κατηγορίες DMARDs σε ασθενείς με νεοπλασία

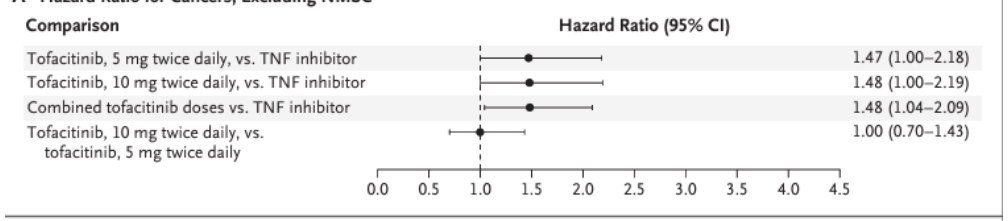
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

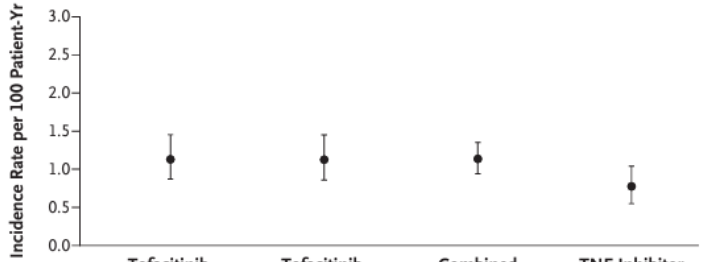
Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis

Steven R. Ytterberg, M.D., Deepak L. Bhatt, M.D., M.P.H., Ted R. Mikuls, M.D., M.S.P.H., Gary G. Koch, Ph.D., Roy Fleischmann, M.D., Jose L. Rivas, M.D., Rebecca Germino, Ph.D., Sujatha Menon, Ph.D., Yanhui Sun, Ph.D., Cunshan Wang, Ph.D., Andrea B. Shapiro, M.D., Keith S. Kanik, M.D., and Carol A. Connell, R.N., Ph.D., for the ORAL Surveillance Investigators*

A Hazard Ratio for Cancers, Excluding NMSC

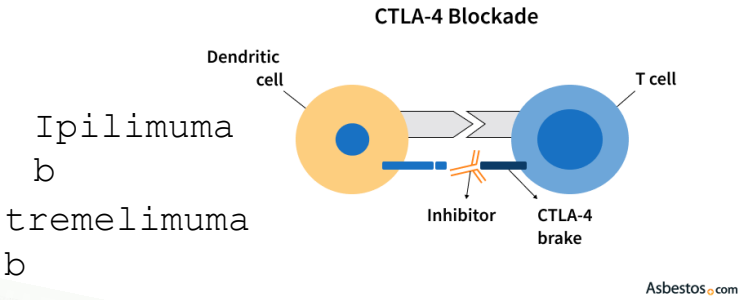


B Incidence Rate for Cancers, Excluding NMSC



No. of Patients with First Event/Total No. (%)	62/1455 (4.3)	60/1456 (4.1)	122/2911 (4.2)	42/1451 (2.9)
No. of Patient-Yr	5491.48	5311.71	10,803.19	5482.30
Incidence Rate per 100 Patient-Yr (95% CI)	1.13 (0.87–1.45)	1.13 (0.86–1.45)	1.13 (0.94–1.35)	0.77 (0.55–1.04)
NNH (patient-yr) vs. TNF Inhibitor	276	275	—	—
NNH (over 5-yr period) vs. TNF Inhibitor	55	55	—	—

Ytterberg SR. et al. N Engl J Med 2022;386:316-26



Ipilimumab

tremelimumab

PTC 5. In patients with a history of cancer, JAK inhibitors and Abatacept may be used with caution, and only in the absence of therapeutic alternatives

- Considering abatacept in patients with RA and **no history of cancer**, 6 observational studies showing in 5/6 a mild but significant increase of incidence of cancer

Study	Type of cancer	Adjusted HR (95% CI) / bDMARDS unless specifed
Ozen et al.	Overall malignancy	1.89 (0.93, 3.82)
Montastruc et al.	Overall malignancy	1.17 (1.06, 1.30) 1.20 (1.03, 1.39)
Simon et al.	Overall malignancy	1.02 (1.09, 1.16)
De Germay et al.	Melanoma	reported odds ratio, 1.58 (1.17, 2.08)
Wadstrom et al.	Squamous cell skin cancer	2.12 (1.14, 3.95) compared with anti-TNF
Huss et al.	Total malignancy	1.8 (1.2, 2.6) compared with b/ts DMARD naive after 2-5 years of active treatment

Ozen, Arthritis Res Ther 2019, Montastruc et al. Rheumatology 2019, Simon et al. Arthritis Res Ther 2019, de Germay et al. Rheumatology 2020, Wadstrom, et al. JAMA Int Med 2017, Huss et al, Rheumatology 2022

Ποια θεραπεία να προτιμήσω τελικά σε ασθενείς με νεοπλασία

PTC 6. When targeted antirheumatic therapy is indicated in patients with a history of solid cancer *, anti-cytokine bDMARDs ** may be preferred over other treatment options

*do not concern melanoma

**anti-cytokine bDMARDs refers to anti-TNF and anti-IL-6 receptor therapy, with clinical evidence for anti-TNF (6 studies) and only translational research data for anti-IL6R

TNFi :

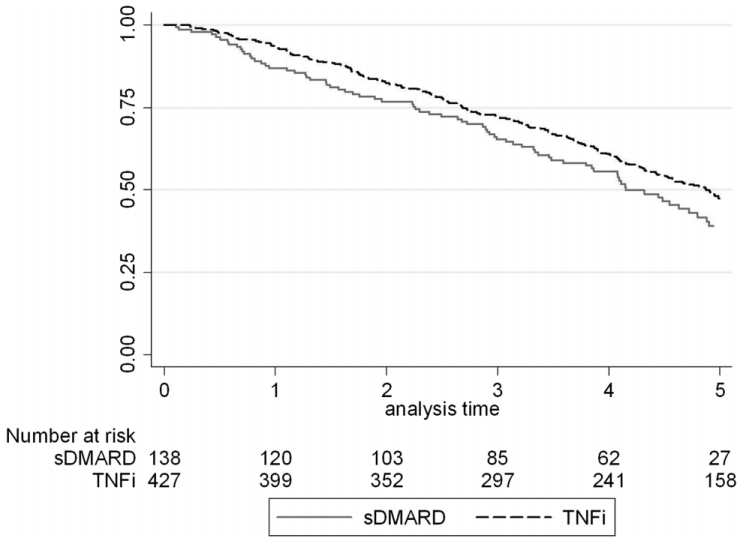
- Registries
- RWE

Clinical and epidemiological research

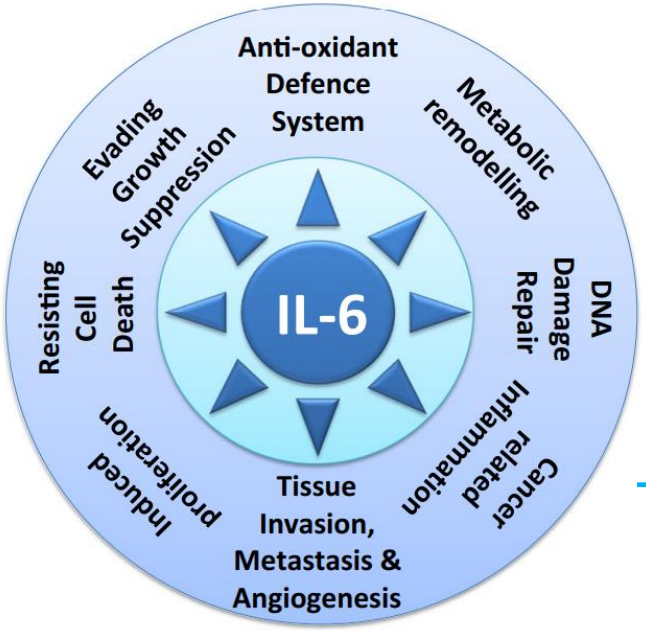
EXTENDED REPORT

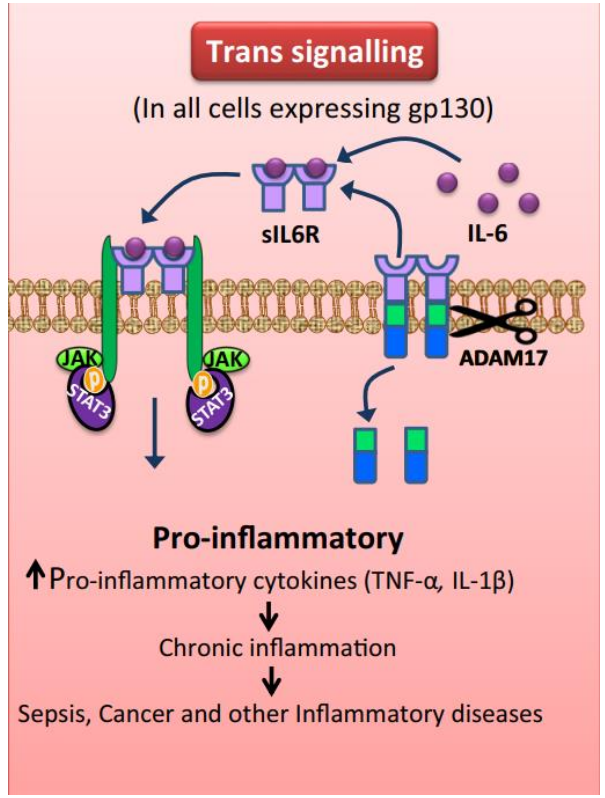
Risk of solid cancer in patients exposed to anti-tumour necrosis factor therapy: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis

Louise K Mercer, Mark Lunt, Audrey L S Low, William G Dixon, Kath D Watson, Deborah P M Symmons, Kimme L Hyrich, BSRBR Control Centre Consortium



Mercer LK, Lunt M, Low ALS, et al. Ann Rheum Dis





IL6 :

- Translational research
- Investigating therapy

Kumari N, Dwarakanath BS, Das A, Bhatt AN.Tumour Biol. 2016

Recommendation

OPEN ACCESS

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]

Table 1 Overarching principles and points to consider for the diagnosis and management of rheumatic irAEs

		LoE	GoR	LoA (0–10) mean (SD)
Overarching principles				
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)

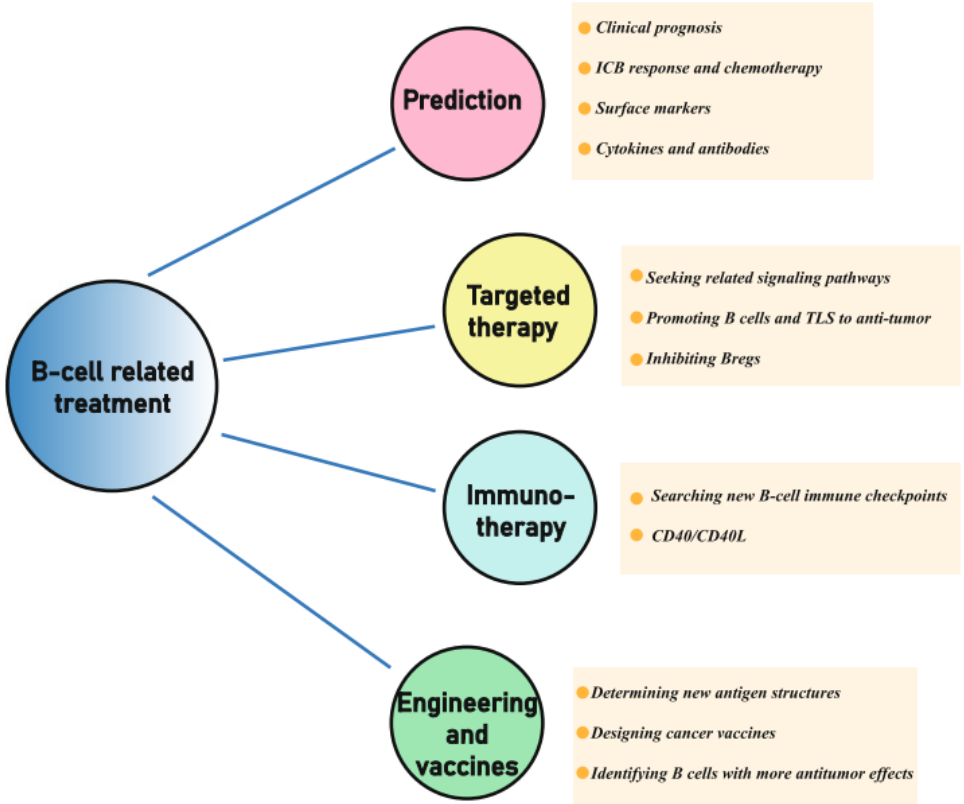
Kostine M,Finckh A, Bingham 3rd CO,et al. Ann Rheum Dis2021;80:36–48

Το RTX ως θεραπεία σε ασθενείς με προϋπάρχουσα νεοπλασία

PTC 7. When targeted anti-rheumatic therapy is indicated in patients with a history of lymphoma, B cell depleting therapy may be preferred over other treatment options.

ΟΜΩΣ: *Για τις νεοπλασίες συμπαγών οργάνων δεν συστήνεται έναντι των TNFi & IL6i*

- ✓ *Β λεμφοκύτταρα περιξ των συμπαγών όγκων προδιαθέτουν για ευνοϊκότερη πρόγνωση*
- ✓ *Η λειτουργία των CPI (και των νεότερων εμβολίων) εξαρτάται από τα Β λεμφοκύτταρα*
- ✓ *Η αντιγονοπαρουσίαση είναι σημαντική στην αναγνώριση νεοπλασματικών κυτταρων*



Zhang, E., Ding, C., Li, S. et al. Biomark Res 11, 28

Οι IL17i σε ασθενείς με νεοπλασία…;

frontiers | Frontiers in Immunology

TYPE Review
PUBLISHED 13 March 2023

The role of Th-17 cells and IL-17 in the metastatic spread of breast cancer: As a means of prognosis and therapeutic target

Tewodros Shibabaw[1], Banchamlak Teferi[2] and Birhanu Ayelign[3,4]*

Types of cytokines	Cellular source	Types of study	Cell lines	Response on IL-17 exposure	Cellular mechanisms
IL-17A	Th-17, TAM, CAF	Preclinical and clinical	MCF7, T47D, BT20, MDA-MB468, MD-MB157, MDA-MB231	Pro-tumorigenesis	Activation or ERK1/2 pathway induces proliferation, migration, invasion, and chemoresistance Recruitment of macrophages, activation of MMP
IL-17A	Th-17, TAM, CAF	Clinical	None	Pro-tumorigenesis	IL-17A associated to MMP-1, 2, 3, 9, and 11 mononuclear infiltrating cells which are correlated to metastasis
IL-17A	Th-17, TAM, CAF	Preclinical	MCF7	Pro-tumorigenesis	Activation of MAPK: MEKK, ERK, JNK, cJun, STAT3 Cell proliferation
IL-17E	Th-17	Preclinical	MCF7, MDA-MB468, MDA-MB 435-S, MDA-MB231, SKBR3, T47D, ZR75, Hs578t, HCC1937, MDA-MB175-7	Anti-tumorigenesis	Induction of apoptosis, decrease in colony formation and tumor growth
IL-17A and IL-17E	Th-17 cell,	Preclinical and clinical	47D, MCF7, BT20, IJG-1731	Pro-tumorigenesis	Activation of cRAF and S6 kinases and *via* chemoresistance
IL-17B	Th-17 cell	Preclinical and clinical	MCF7, MDA-MB-157, MDA-MB-231, MDA-MB-361, BT20	Pro-tumorigenesis	Resistance to paclitaxel in cell lines *via* ERK pathway Upregulation of BCL2 promotion of proliferation and tumor growth through IL-17RB *via* NF-kB and TRAF6
IL-17E	Th-17 cell	Preclinical study	MCF7, MDA-MB468, MDA-MB 435-S, MDA-MB231, SKBR3, T47D, ZR75, Hs578t, HCC1937, MDA-MB175-7	Anti-tumorigenesis	Induction of apoptosis, decrease in colony formation and tumor growth

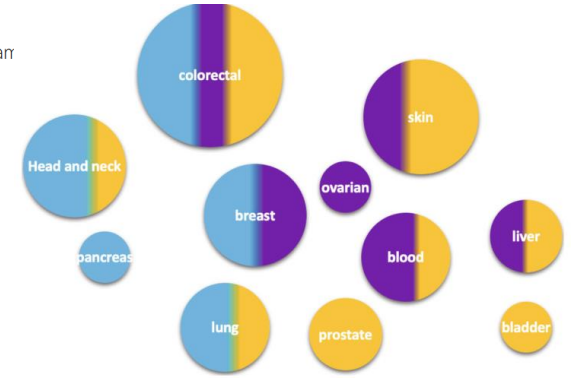
Mikkola *et al. BMC Cancer* (2022) 22:54
https://doi.org/10.1186/s12885-021-08969-0

BMC Cancer

RESEARCH Open Access

Variable roles of interleukin-17F in different cancers

Tiina Mikkola[1,2], Rabeia Almahmoudi[1,2], Tuula Salo[1,2,3,4,5] and Ahmed Al-Sam



Open access Original research

Journal for ImmunoTherapy of Cancer

Blocking IL-17A enhances tumor response to anti-PD-1 immunotherapy in microsatellite stable colorectal cancer

Chao Liu,[1,2] Ruiqi Liu,[3] Bojun Wang,[1] Jie Lian,[1] Yang Yao,[1] Haoxiu Sun,[4] Chunhui Zhang,[1] Lin Fang,[1] Xin Guan,[1] Jiaqi Shi,[1] Shuling Han,[1] Fei Zhan,[1] Shengnan Luo,[1] Yuanfei Yao,[1,2] Tongsen Zheng,[1,5] Yanqiao Zhang [1,2]

protumorigenic ●no association found

nature cancer

Article https://doi.org/10.1038/s43018-023-00610-2

Interleukin 17 signaling supports clinical benefit of dual CTLA-4 and PD-1 checkpoint inhibition in melanoma

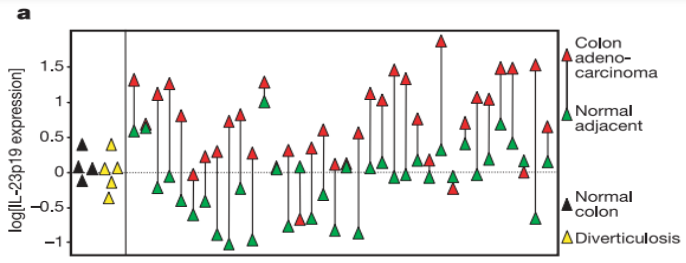
Οι IL23i σε ασθενείς με νεοπλασία

Vol 442|27 July 2006|doi:10.1038/nature04808 nature

LETTERS

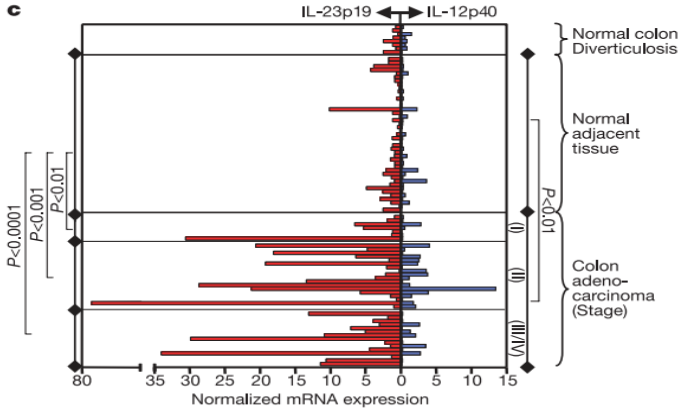
IL-23 promotes tumour incidence and growth

John L. Langowski[1]*, Xueqing Zhang[1]*, Lingl
Beth Basham[1], Terrill McClanahan[1], Robert



b

Cancer type	Number of paired (tumour and normal) samples	Fold increase in expression: Average	Number >5×	Number >10×	P
Colon	36	15.33	23	17	0.0001
Ovarian	32	9.45	12	4	0.0001
Head and neck	44	3.41	11	4	0.01
Lung	114	3.03	20	8	0.0001
Breast	78	2.86	16	6	0.0001
Stomach	64	2.13	9	3	0.001
Melanoma	89	1.47	5	0	0.0001



igure 1 | Overexpression of IL-23 but not of IL-12 in human cancer.

NATURE| Vol 442|27 July

nature immunology

Article

https://doi.org/10.1038/s41590-024-01755-7

IL-23 stabilizes an effector T_{reg} cell program in the tumor microenvironment

Nature Immunology | Volume 25 | March 2024 | 512–524

PNAS RESEARCH ARTICLE | IMMUNOLOGY AND INFLAMMATION

Antibody-mediated blockade of the IL23 receptor destabilizes intratumoral regulatory T cells and enhances immunotherapy

Andrew E. Wight[a,b,1], Jessica M. Sido[a,b,1], Sandrine Degryse[a,b], Lin Ao[a,b], Hidetoshi Nakagawa[a,b], Yiguo Qiu(Vivian)[a,b], Xianli Shen[a,b], Oba Oseghali[a], Hye-Jung Kim[a,b], and Harvey Cantor[a,b,2]

PNAS Vol. 119 | No. 18 May 3, 2022

- Η IL23 σταθεροποιεί το μικροπεριβάλλον των Tregs που αντιστέκονται στην καταστολή του όγκου
- Κατάργηση της σηματοδότησης της IL23 κάνει τον όγκο πιο ευάλωτο στο

Ακόμα έχουμε πολλά να μάθουμε για την χρήση των DMARDs σε ασθενείς με νεοπλασίες…

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

Combining Nivolumab and Ipilimumab with Infliximab or Certolizumab in Patients with Advanced Melanoma: First Results of a Phase Ib Clinical Trial

Anne Montfort[1,2], Thomas Filleron[3,4], Mathieu Virazels[1,2], Carine Dufau[1,2,5], Jean Milhès[1,2], Cécile Pagès[4,6], Pascale Olivier[7], Maha Ayyoub[1,4,5], Muriel Mounier[3,4], Amélie Lusque[3,4], Stéphanie Brayer[1,2,6], Jean-Pierre Delord[1,4,5], Nathalie Andrieu-Abadie[1,2], Thierry Levade[1,2,5,8], Céline Colacios[1,2,5], Bruno Ségui[1,2,5], and Nicolas Meyer[1,2,4,5,6]

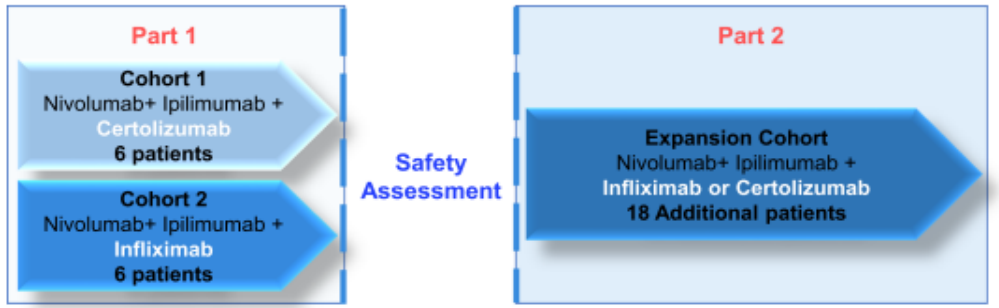
ABSTRACT

Purpose: TNF blockers can be used to manage gastrointestinal inflammatory side effects following nivolumab and/or ipilimumab treatment in patients with advanced melanoma. Our preclinical data showed that anti-TNF could promote the efficacy of immune checkpoint inhibitors.

Results: Only one dose-limiting toxicity was observed in the infliximab cohort. The two different combinations were found to be safe. We observed lower treatment-related AEs with infliximab as compared with certolizumab. In the certolizumab cohort, one patient was not evaluable for response. In this cohort, four of eight

TNF-Inhibitor as Immune Checkpoint Inhibitor for Advanced MELanoma (TICIMEL)
Clinical Trial Identifier: NCT03293784

A



B

	Induction Phase				Maintenance Phase			
Week	0	3	6	9	12	14	16	Continued…
Day	1	22	43	64	85	99	112	
Nivolumab (IV)	1 mg/kg	1 mg/kg	1 mg/kg	1 mg/kg	3 mg/kg	3 mg/kg	3 mg/kg	3 mg/kg Q2W
Ipilimumab (IV)	3 mg/kg	3 mg/kg	3 mg/kg	3 mg/kg	-	-	-	-
Certolizumab (SC)	400 mg	400 mg	400 mg	200 mg	200 mg	200 mg	200 mg	200 mg Q2W
Infliximab (IV)	5 mg/kg	5 mg/kg	5 mg/kg	-	-	5 mg/kg	-	5 mg/kg Q8W

End of DLT period evaluation

frontiers in Immunology

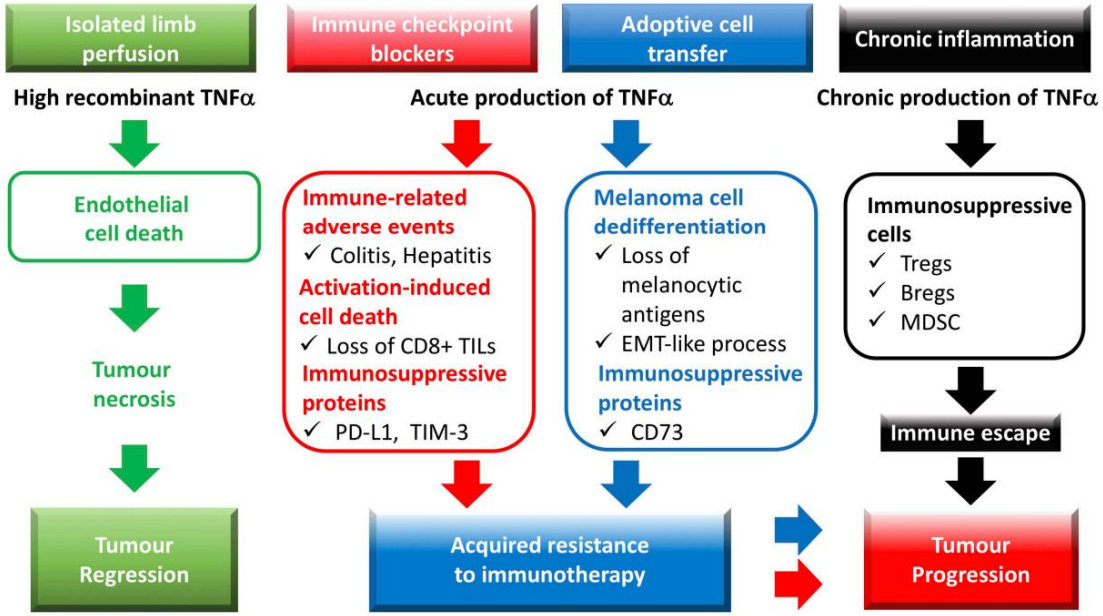
OPINION
published: 31 July 2019
doi: 10.3389/fimmu.2019.01818

The TNF Paradox in Cancer Progression and Immunotherapy

Anne Montfort[1], Céline Colacios[1,2], Thierry Levade[1,2,3], Nathalie Andrieu-Abadie[1], Nicolas Meyer[1,2,4] and Bruno Ségui[1,2]*

[1] INSERM UMR 1037, Cancer Research Center of Toulouse (CRCT), Toulouse, France, [2] Université Toulouse III - Paul Sabatier, Toulouse, France, [3] Laboratoire de Biochimie, Institut Fédératif de Biologie, CHU Purpan, Toulouse, France, [4] Dermatologie, Institut Universitaire du Cancer (IUCT-O) et CHU de Toulouse, Toulouse, France

Keywords: tumor necrosis factor (TNF), PD-1, CTLA-4, melanoma, immune escape



Και ορισμένα νέα δεδομένα και στρατηγικές ίσως μας αφήσουν έκπληκτους !!!

Science **Ruxolitinib** Current Issue First release papers Archive About

HOME > SCIENCE > VOL. 384, NO. 6702 > JAK INHIBITION ENHANCES CHECKPOINT BLOCKADE IMMUNOTHERAPY IN PATIENTS WITH HODGKIN LYMPHOMA

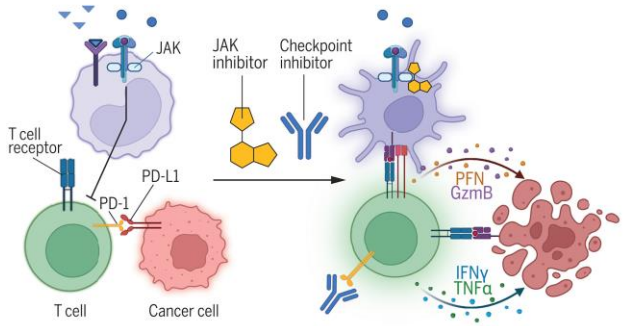
RESEARCH ARTICLE | CLINICAL TRIALS

JAK inhibition enhances checkpoint blockade immunotherapy in patients with Hodgkin lymphoma

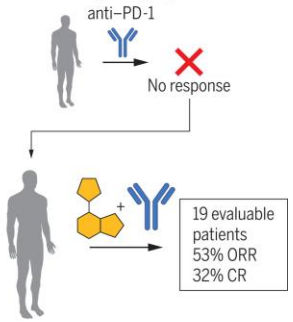
JAROSLAV ZAK, ISARAPHORN PRATUMCHAI, BRETT S. MARRO, KRISTI L. MARQUARDT, REZA BEHESHTI ZAVAREH, LUKE L. LAIRSON, MICHAEL B. A. OLDSTONE, JUDITH A. VARNER, LIVIA HEGEROVA, [...], AND JOHN R. TEIJARO +4 authors Authors Info & Affiliations

SCIENCE · 21 Jun 2024 · Vol 384, Issue 6702 · DOI: 10.1126/science.ade8520

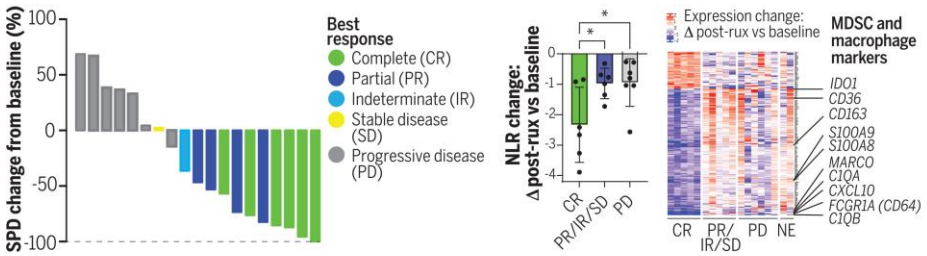
JAK inhibition with checkpoint inhibitors reprograms myeloid cells from a suppressive to an immunostimulatory state



Ruxolitinib with nivolumab in anti–PD-1 relapsed or refractory Classical Hodgkin lymphoma



Neutrophil and suppressive myeloid cell reductions correlate with response



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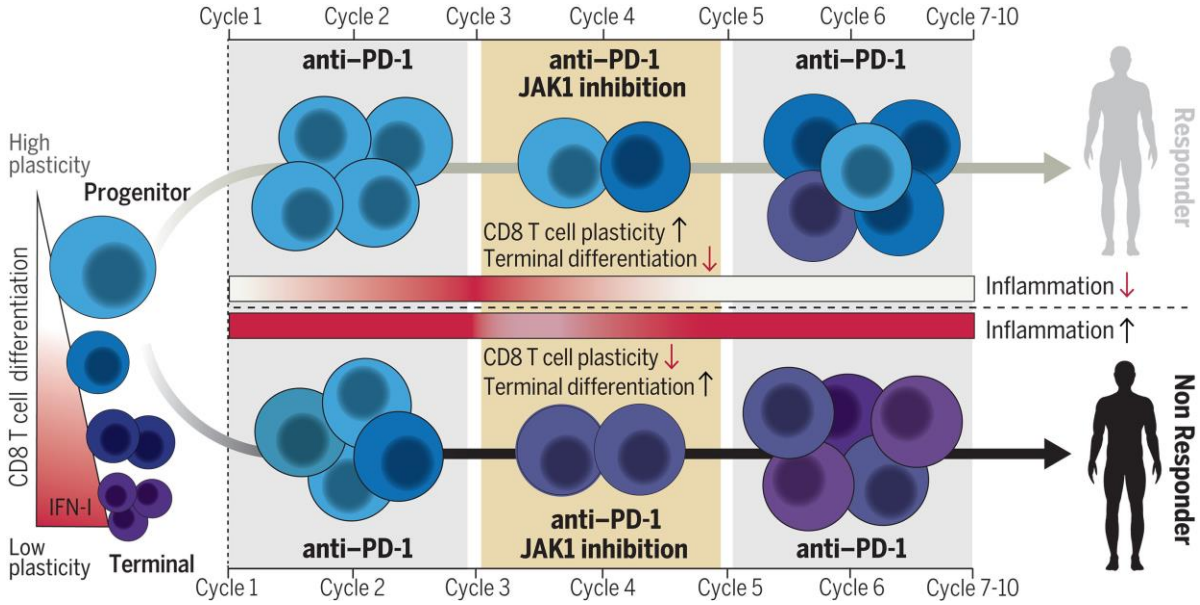
HOME > SCIENCE > VOL. 384, NO. 6702 > COMBINED JAK INHIBITION AND PD-1 IMMUNOTHERAPY FOR NON–SMALL CELL LUNG CANCER PATIENTS

RESEARCH ARTICLE | CLINICAL TRIALS

Combined JAK inhibition and PD-1 immunotherapy for non–small cell lung cancer patients

DIVIJ MATHEW, MELINA E. MARMARELIS, CAITLIN FOLEY, JOSHUA M. BAUML, DARWIN YE, REEM GHINNAGOW, SHIN FOONG NGIOW, MAX KLAPHOLZ, SOYEONG JUN, [...], AND ANDY J. MINN +12 authors Authors Info & Affiliations

SCIENCE · 21 Jun 2024 · Vol 384, Issue 6702 · DOI: 10.1126/science.adf1329



Συμπεράσματα

- Η χρήση των DMARDs σε ασθενείς με προηγούμενη νεοπλασία:
  - Συν-αποφασίζεται με ογκολόγο και ασθενή
  - Εξατομίκευση ανάλογα με ενεργότητα νόσου και υποκείμενη νεοπλασία
  - Η νεοπλασία είναι σε ύφεση (με ή χωρίς θεραπεία) και η ρευματική νόσος σε έξαρση
  - Η έναρξη της θεραπείας μπορεί να γίνει άμεσα

- Σε συμπαγείς όγκους προτιμώνται οι θεραπείες έναντι κυτταροκινών (TNF, IL6) vs συστηματικές θεραπείες (RTX,ABA)

- Στο λέμφωμα προτιμάται το RTX

- Οι IL17i και IL23 φαίνεται να προσφέρουν πλεονέκτημα σε κάποια «μοντέλα» νεοπλασιών, αλλά δεν υπάρχουν δεδομένα σε ανθρώπους για να το υποστηρίξουν

- Οι JAK αναστολείς δεν συστήνονται προς το παρόν, ειδικά σε ηλικιωμένους ασθενείς