Jan 2024 ONC-BE-2300241

What's new in immunotoxicity?

ISA meeting 10 jan 2024

Sandrine Aspeslagh, MD, PhD

ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

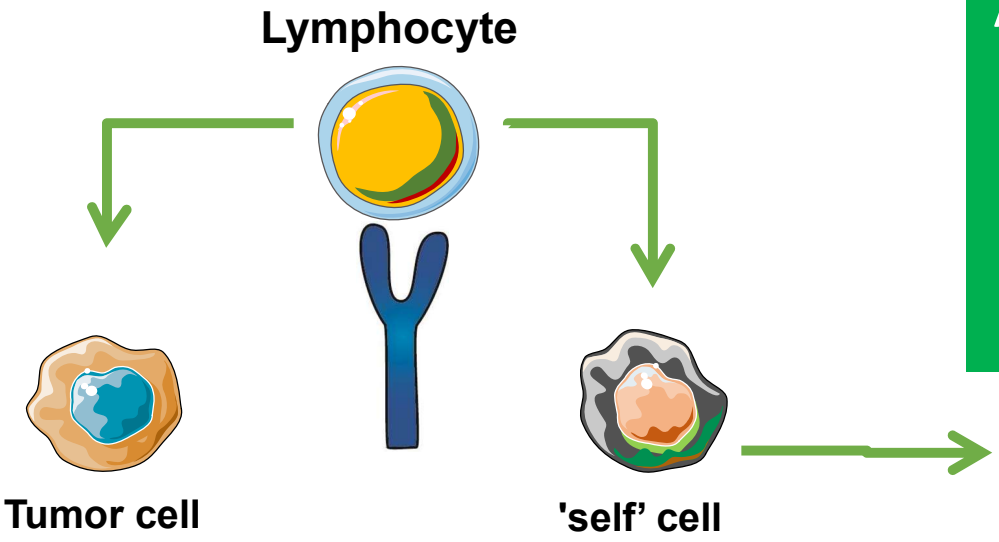
Micros & question cards available during workshop for the Q&A at the end

ImmunoScience Academy

With the support of Bristol Myers Squibb

BACKGROUND IMMUNE CHECKPOINT INHIBITION

Only immunity against cancer cells?



Autoimmune-like syndromes called immune-related adverse events (irAEs)

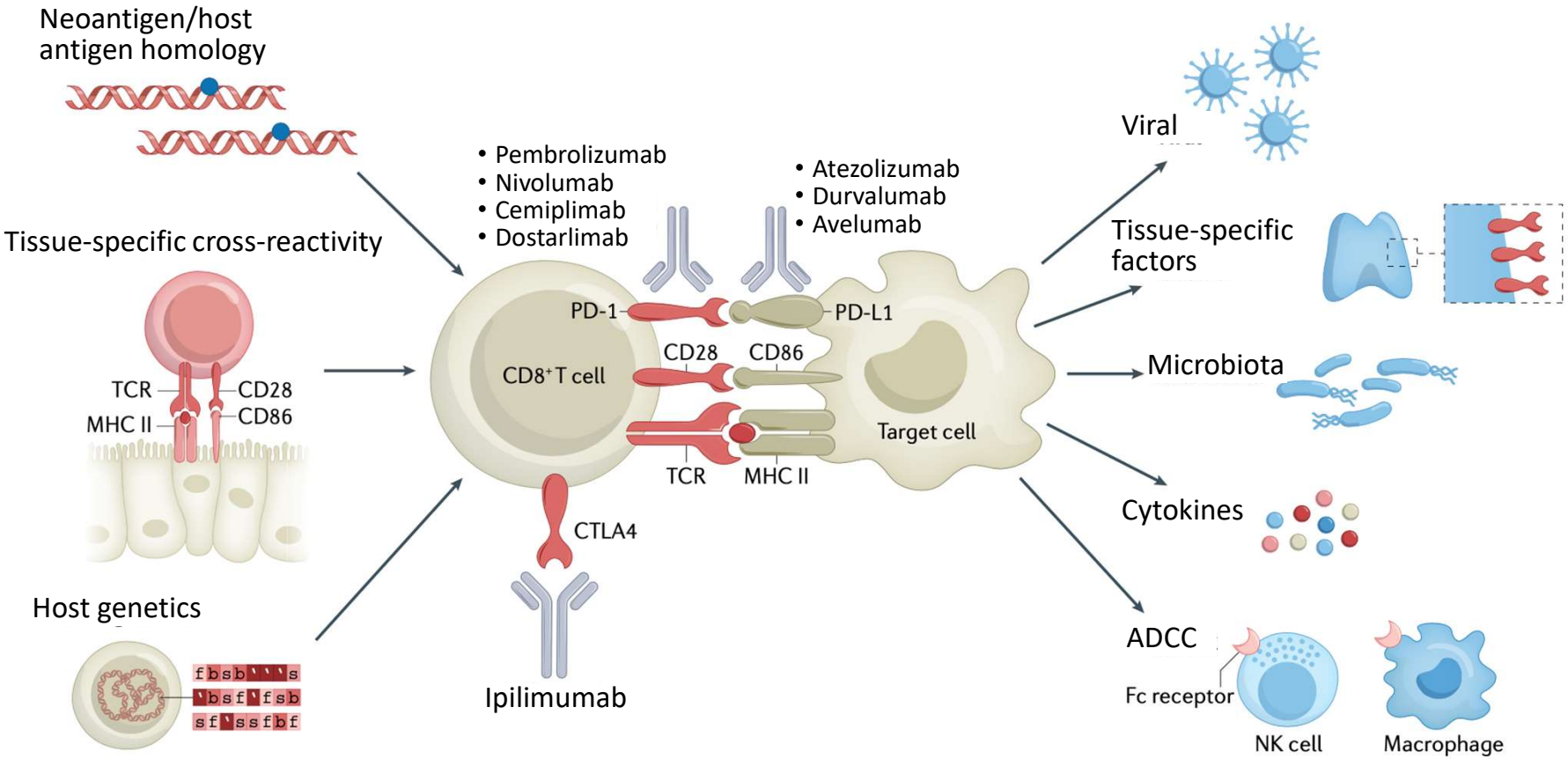
Most commonly occur in first 3 months

irAE, immune-related adverse event.

irAE pathophysiology: largely unknown

TUMOR SPECIFIC

NON-TUMOR SPECIFIC

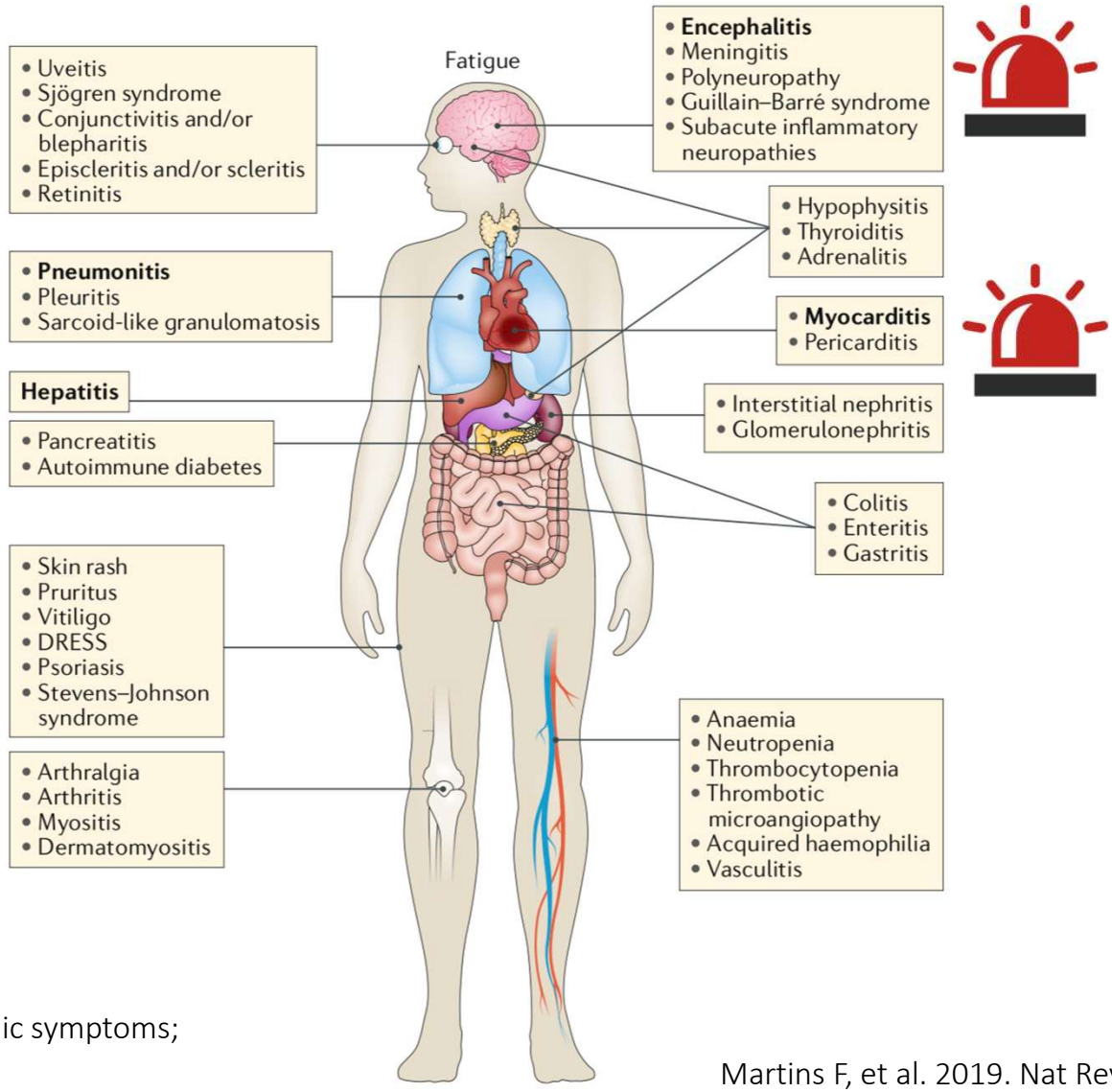


ADCC, antibody-dependent cellular cytotoxicity; irAE, immune-related adverse event.

Johnson DB, et al. 2022. Nat Rev Clin Oncol.

All organs can be affected by irAEs

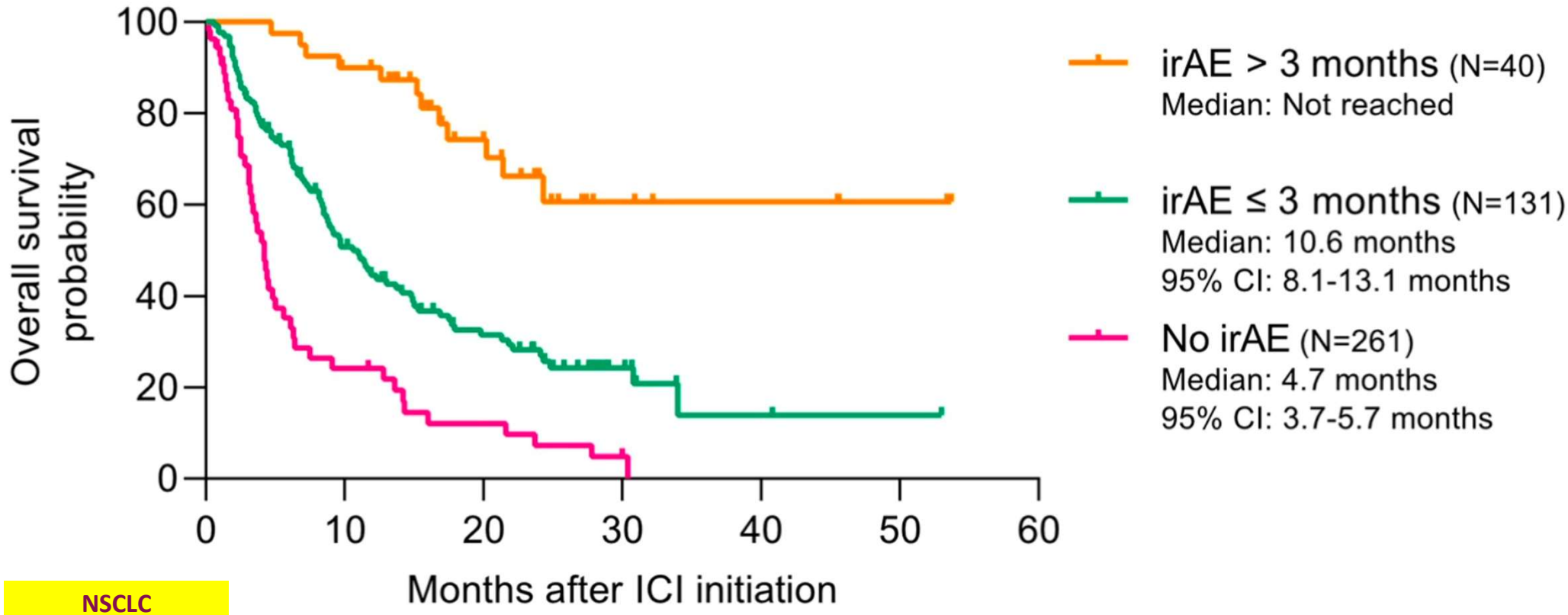
- Diverse
- Rare
- Manageable



DRESS, drug reaction with eosinophilia and systemic symptoms; irAE, immune-related adverse event.

Martins F, et al. 2019. Nat Rev Clin Oncol.

irAEs can be good news



NSCLC

CI, confidence interval; ICI, immune checkpoint inhibitor;
irAE, immune-related adverse event.

Hsiehchen D, et al. 2022. Oncoimmunology.

irAE and tumor outcome

Treatment effect in the presence and absence of irAEs

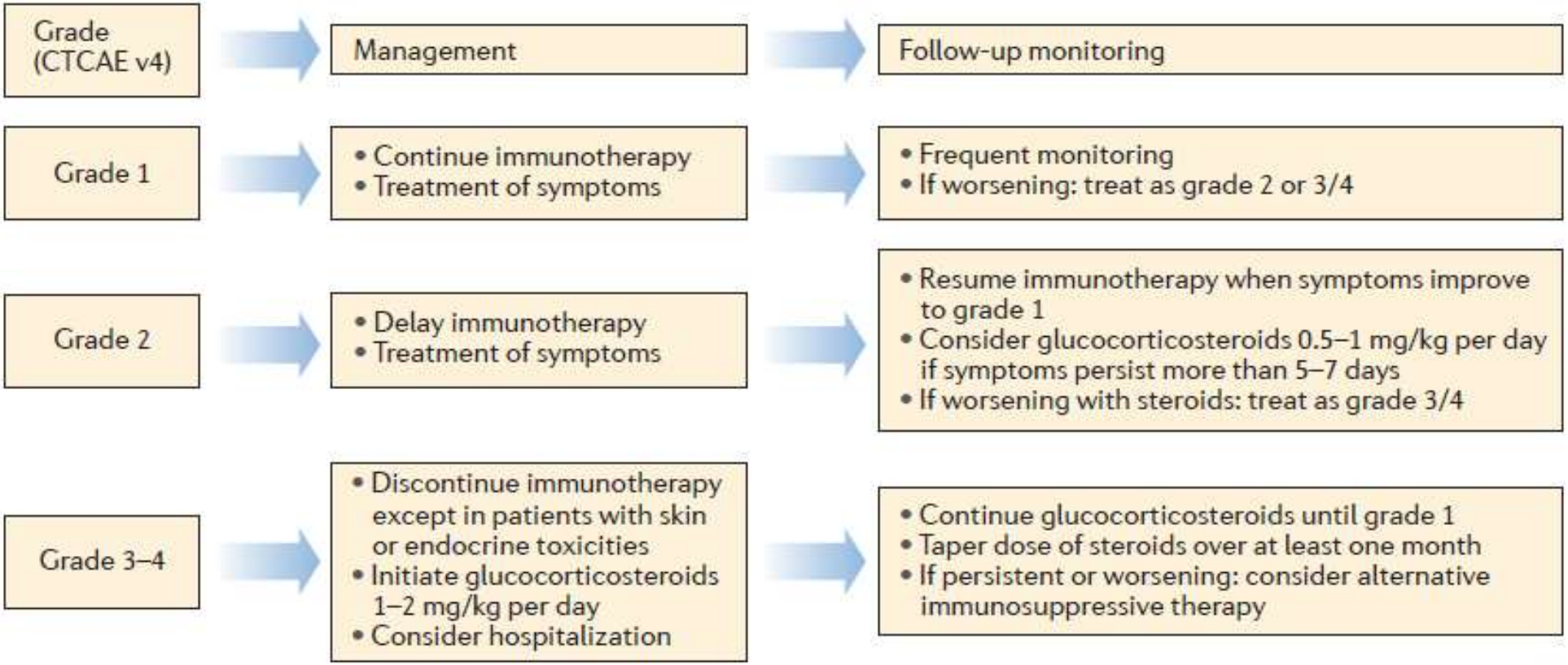
Immune-Related Adverse Event Status and Treatment Arm	Recurrence-Free Survival, HR (95% CI)[a]	*P* Value[a,b]
Any irAE		
Placebo	1	
Pembrolizumab without/before irAE	0.62 (0.49-0.78)	.03
Pembrolizumab after irAE onset	0.37 (0.24-0.57)	
Endocrine irAE		
Placebo	1	
Pembrolizumab without/before irAE	0.60 (0.48-0.75)	.03
Pembrolizumab after irAE onset	0.34 (0.20-0.57)	
Vitiligo		
Placebo	1	
Pembrolizumab without/before irAE	0.57 (0.46-0.70)	.15
Pembrolizumab after irAE onset	0.13 (0.02-0.95)	
Any severe (grade 3-4) irAE		
Placebo	1	
Pembrolizumab without/before irAE	0.55 (0.44-0.68)	.43
Pembrolizumab after irAE onset	0.78 (0.32-0.91)	

MELANOMA

CI, confidence interval; HR, hazard ratio; irAE, immune-related adverse event.

Eggermont AMM, et al. 2020. JAMA Oncol.

Severity and treatment



Boutros C, et al. 2016. Nat Rev Clin Oncol.

Belgian Multidisciplinary Immunotoxicity Board (BITOX)

Agenda →

How to present a case →

People →

Joint pathology →

Colitis →

Skin toxicity →

Hepatic toxicity →

Nephrotoxicity →

Neurologic toxicity →

Pneumonitis →

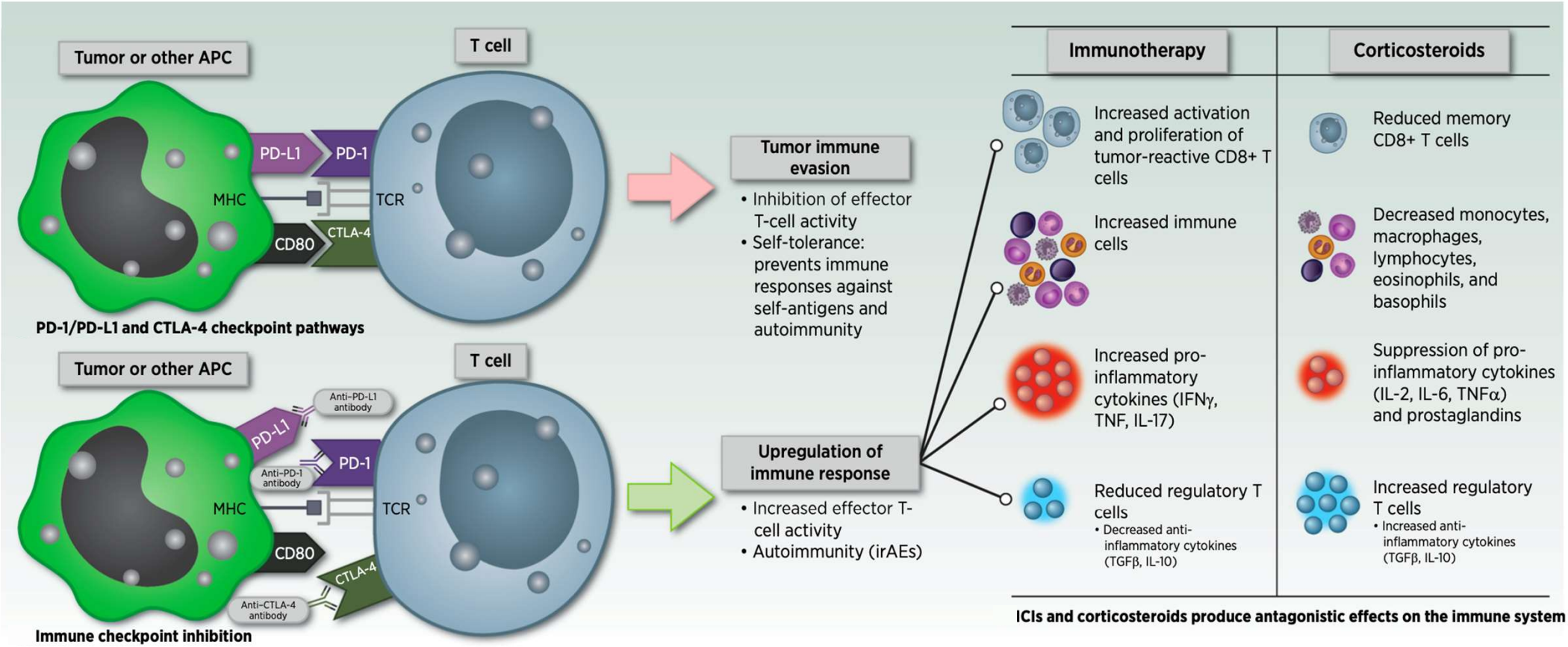
Endocrine toxicity →

Muscle pathology →

Immune Checkpoint Inhibition in combination with TKI

Axitinib + anti-PD-(L)1

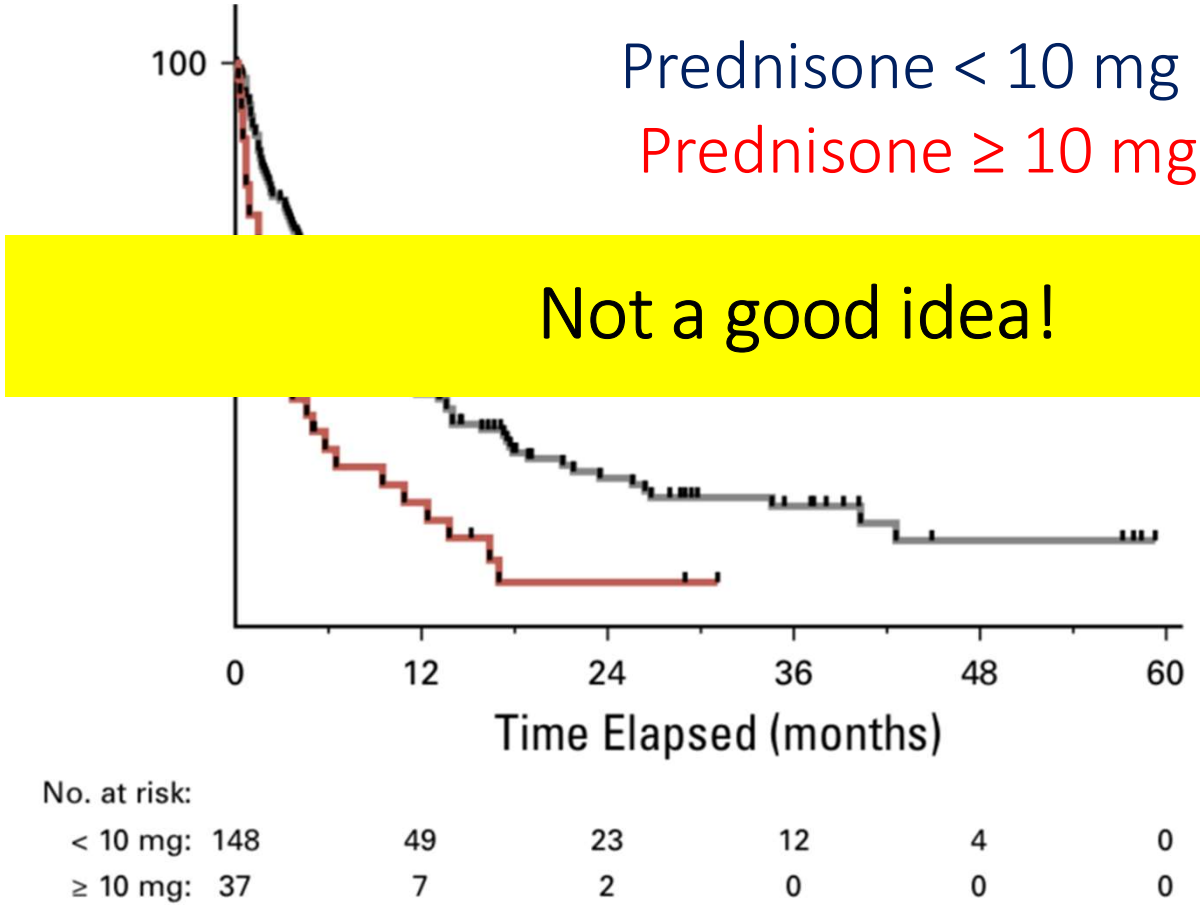
https://www.bsmo.be/immunomanager/start/



APC, antigen-presenting cell.

Goodman RS, et al. 2023. Clin Cancer Res.

Corticosteroids to support quality of life



Prednisone < 10 mg (n=148)

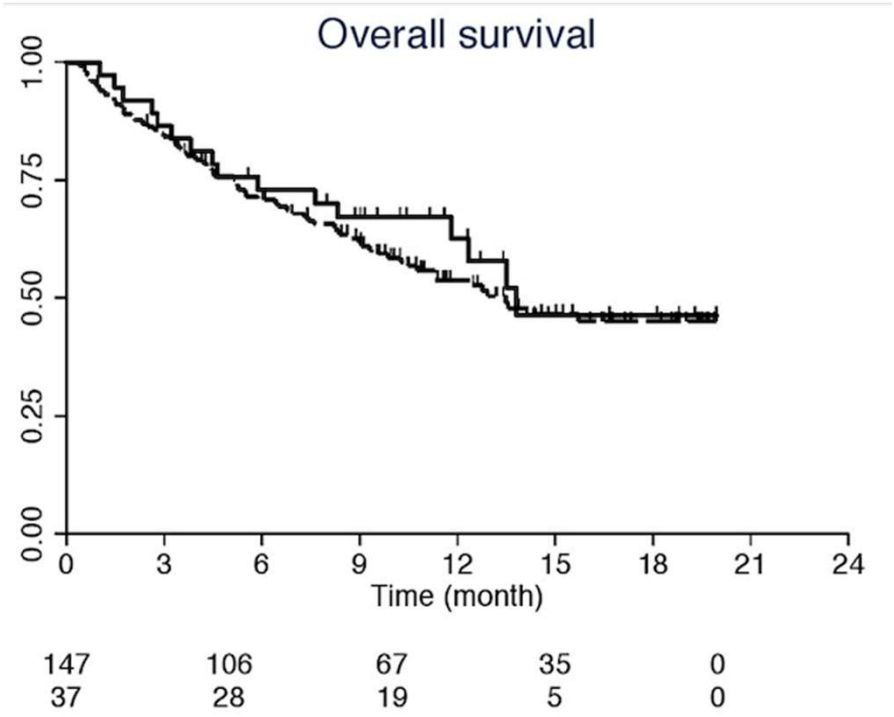
Prednisone ≥ 10 mg (n=37)

Not a good idea!

OS, overall survival.

Arbour KC, et al. 2018. J Clin Oncol.

What is the effect of corticoids given for irAE on the anti-tumor response?



All ok
Slides on the side can be taken away

Corticoids
No corticoids

Higashiyama RI, et al. 2018. Presentation at ASCO-SITC Clinical Immuno-Oncology Symposium.

Early Use of High-Dose Glucocorticoid for the Management of irAE Is Associated with Poorer Survival in Patients with Advanced Melanoma Treated with Anti–PD-1 Monotherapy

Xue Bai[1,2], Jiani Hu[3], Allison Betof Warner[4], Henry T. Quach[5], Christopher G. Cann[5], Michael Lu Si[1], Bixia Tang[1], Chuanliang Cui[1], Xiaoling Yang[1,6], Xiaoting Wei[1], Lalit Pallan[7], Catriona Ha Michael P. Manos[8], Olivia Ouyang[8], Michelle S. Kim, Gyulnara Kasumova, Justine V. Cohen[2], Donald P. Lawrence[2], Christine Freedman[2], Riley M. Fadden[2], Krista M. Rubin[2], Tatyana Sha Dennie T. Frederick[9], Keith T. Flaherty[2,10], Osama E. Rahma[8,10], Georgina V. Long[7,10], Alexander M. Menzies[7,10], Jun Guo[1,10], Alexander N. Shoushtari[4,10], Douglas B. Johnson[5,10], Ryan J. Sullivan[2,10], and Genevieve M. Boland[9,10]

Article

Better Late Than Never: The Impact of Steroidal Treatment on the Outcome of Melanoma Patients Treated with Immunotherapy

Neta Bar-Hai [1], Guy Ben-Betzalel [1], Ronen Stoff [1], Shirly Grynberg [1], Jacob Schachter [1,2], Ronnie Shapira-Frommer [1] and Nethanel Asher [1,*]

Sex and anti-inflammatory treatment affect outcome of melanoma and non-small cell lung cancer patients with rheumatic immune-related adverse events

Karolina Gente ,[1] Leonore Diekmann,[1] Lea Daniello,[2,3] Julia Will,[1] Manuel Feisst,[4] Victor Olsavszky,[5] Janine Günther,[1] Hanns-Martin Lorenz,[1] M Margarida Souto-Carneiro,[1] Jessica C Hassel ,[6] Petros Christopoulos,[2,3] Jan Leipe[7]

Think before starting corticoids!!
In case of doubt, discuss with multidisciplinary team
General trend:
- -irAE are less chronic than their AID counterpart syndrome
- -irAE react better to corticoids than their AID counterpart syndrome

→Taper when irAE has responded to corticoids
→In case of non-response: check diagnosis again and discuss with multidisciplinary team

AID, autoimmune disease; irAE, immune-related adverse event.

Bai X, et al. 2021. Clin Cancer Res. Bar-Hai N, et al. 2023. Cancers (Basel). https://www.bsmo.be/immunomanager/start. Gente K, et al. 2023. J Immunother Cancer.

Position statement on the management of the immune checkpoint inhibitor-induced colitis via multidisciplinary modified Delphi consensus

Valérie Desmedt [a,1], Aranzazu Jauregui-Amezaga [b,c,1], Liselotte Fierens [d], Sandrine Aspeslagh [e], Jeroen Dekervel [f], Els Wauters [g,h], Marc Peeters [i], Joao Sabino [f], Lara Crapé [j], Michael Somers [b], Anne Hoorens [k], Joris Dutré [l], Triana Lobatón [a,m], for BIRD (Belgian IBD Research and Development)Belgian Society of Medical Oncology (BSMO)Belgian group of Digestive Oncology (BGDO)BeRS (Belgian Respiratory Society)On behalf of the participants of the collaborator group in the modified Delphi consensus for the Position Statement on the management of the immune checkpoint inhibitor induced colitis [2]

Desmedt V, et al. 2023. Eur J Cancer.

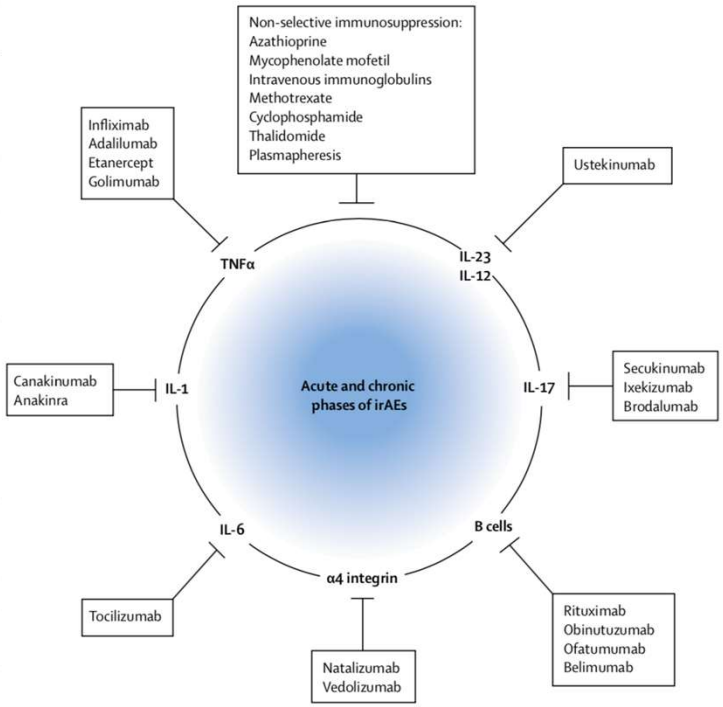
New therapeutic perspectives to manage refractory immune checkpoint-related toxicities

Filipe Martins, Gerasimos P Sykiotis, Michel Maillard, Montserrat Fraga, Camillo Ribi, Thierry Kuntzer, Olivier Michielin, Solange Peters, Georges Coukos, Francois Spertini, John A Thompson, Michel Obeid

	irAE indications
Anti-IL-1 blockade	Severe irAE during acute phase; severe or refractory arthritis; chronic inflammatory; demyelinating polyradiculoneuritis; psoriasis-like reactions; psoriasis exacerbation; severe and anti-TNFα refractory colitis; myasthenia gravis; encephalitis; aseptic meningitis; myocarditis; pneumonitis
Anti-IL-6 blockade	Severe irAE during acute phase; severe or refractory arthritis; large vessel vasculitis; uveitis; myocarditis; pneumonitis; myasthenia gravis
Intravenous immunoglobulins	Guillain-Barré syndrome; subacute and chronic inflammatory demyelinating polyradiculoneuritis; subacute and chronic inflammatory neuropathies; immune neutropenia; immune thrombocytopenia; facial nerve palsy; myasthenia gravis; transverse myelitis; enteric neuropathy; encephalitis; aseptic meningitis
Anti-CD20 depletion	Systemic lupus erythematosus; severe Sjögren's syndrome; ANCA-associated vasculitis; cutaneous vasculitis; autoimmune autonomic ganglionopathy; sensory ganglionopathy; nephritis; myasthenia gravis; transverse myelitis; enteric neuropathy; encephalitis; aseptic meningitis; hepatitis
Anti-IL-17 blockade	Severe colitis and anti-TNFα refractory colitis; severe or refractory arthritis; anti-IL-6 refractory irAEs
Anti-TNFα blockade	Severe colitis; hepatitis; severe or refractory arthritis; nephritis; uveitis; pneumonitis; myocarditis
Anti-integrin 4 blockade	Limbic encephalitis
Anti-IL-23 and anti-IL-12 blockade	Acute phase, severe, or anti-TNFα refractory colitis; severe or anti-TNFα refractory psoriasis; severe or refractory arthritis
Janus kinase inhibitor	Severe or refractory arthritis

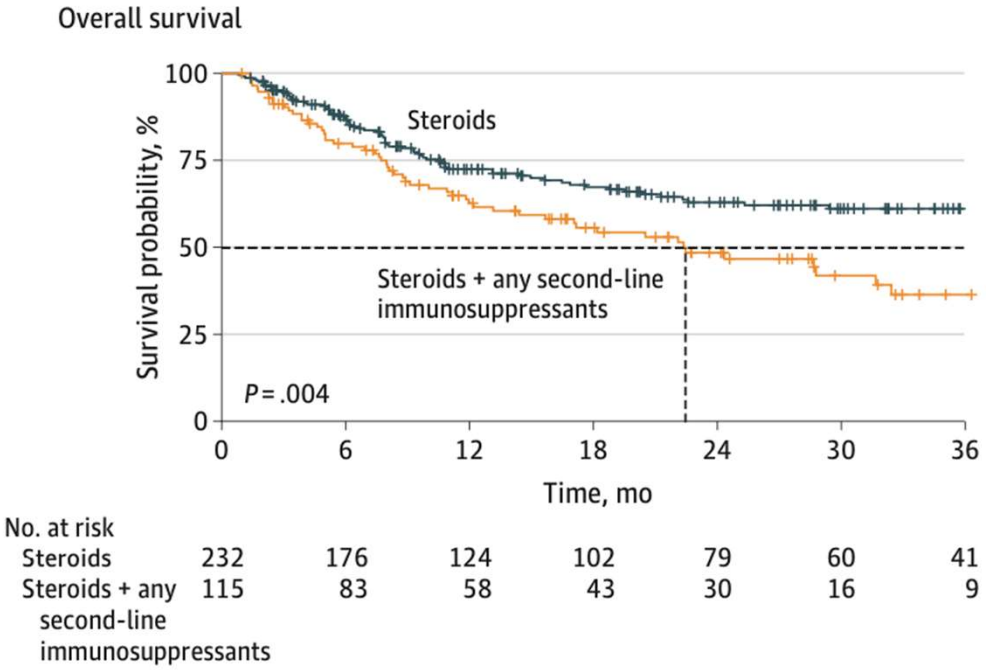
irAE=immune-related adverse event; IL=interleukin type; ANCA=antineutrophil cytoplasmic antibody.

Table: **New therapeutic perspectives for the management of immune-related adverse events**



Martins F, et al. 2019. Lancet Oncol.

What is the effect of other immunosuppressants given for irAE on the anti-tumor response?



Ok slides can be excluded

Corticoids

Corticoids + 2nd line immunosuppressants

The use of 2nd line immunosuppressants should be discussed with the multidisciplinary team

Van Not OJ, et al. 2022. JAMA Oncol.

Arthritis: DMARD or not?

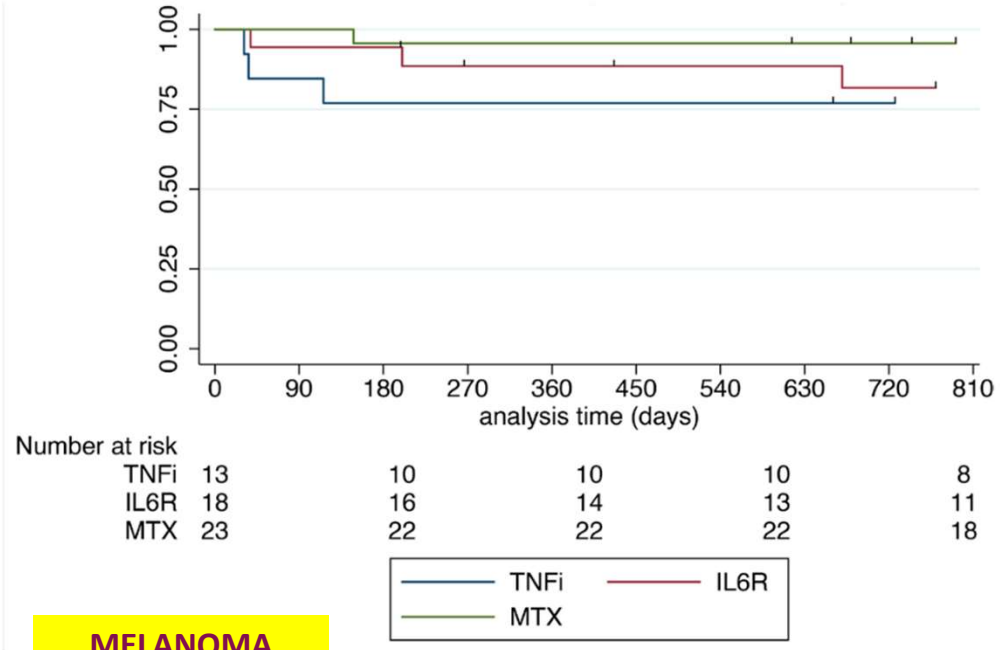
-anti-IL6: best for arthritis

-effect on tumor response may depend on tumor type

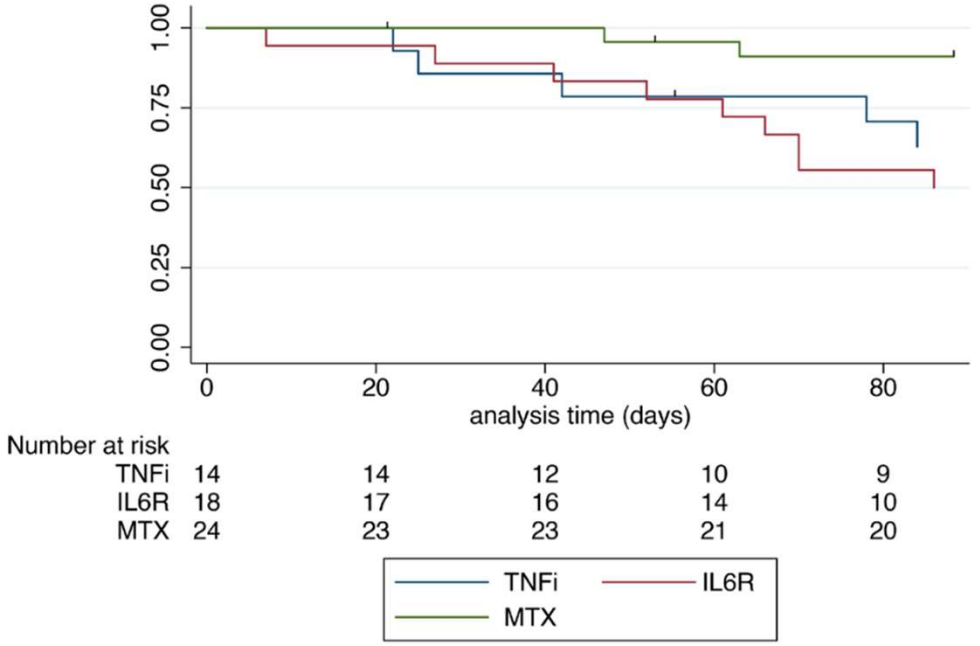
Comparative safety and effectiveness of TNF inhibitors, IL6 inhibitors and methotrexate for the treatment of immune checkpoint inhibitor-associated arthritis

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 [1,2] Divya Rajesh,[9] Carlos Andres Aude [7] Lydia Gedmintas,[10] Lindsey MacFarlane,[10] Senada Arabelovic,[10] Adewunmi Falohun,[3] Komal Mushtaq,[11] Farah Al Haj,[12] Adi Diab,[13] Ami A Shah,[14] Clifton O Bingham [15] Karmela Kim Chan [1,2] Laura C Cappelli [15]

Time to cancer progression from ICI initiation



Time to arthritis control from DMARD initiation



MELANOMA

Other tumor types: MTX > anti-IL6

DMARD, disease-modifying antirheumatic drug; ICI, immune checkpoint inhibitor; IL, interleukin; MTX, methotrexate; TNFi, tumour necrosis factor inhibitor.

Bass AR, et al. 2023. Ann Rheum Dis.

IPI/NIVO/TOCILIZUMAB phase II

- A total of **41 patients**, melanoma stage IV
- Response rate by RECIST is 58%: **higher than** Checkmate-511 (47%)
  - 1/5 stable pts having progressed at a median follow up of 6 months;
  - 3 pts have died so far, all related to progression
- Grade 3-4-5 treatment-related irAE rate: 17%
  - which is lower than expected based on Checkmate-511 at 34%
- 6 pts of 41 have stopped therapy due to grades-2-3-4 irAEs so far = 14%
  - 3 had G3/4 colitis

→ tocilizumab can be discussed in case of steroid refractory irAE

G, grade; ipi, ipilimumab; irAE, immune-related adverse event; nivo, nivolumab; pts, patients; RECIST, response evaluation criteria in solid tumors.

Weber JS, et al. 2021. Presentation at the ESMO Congress.

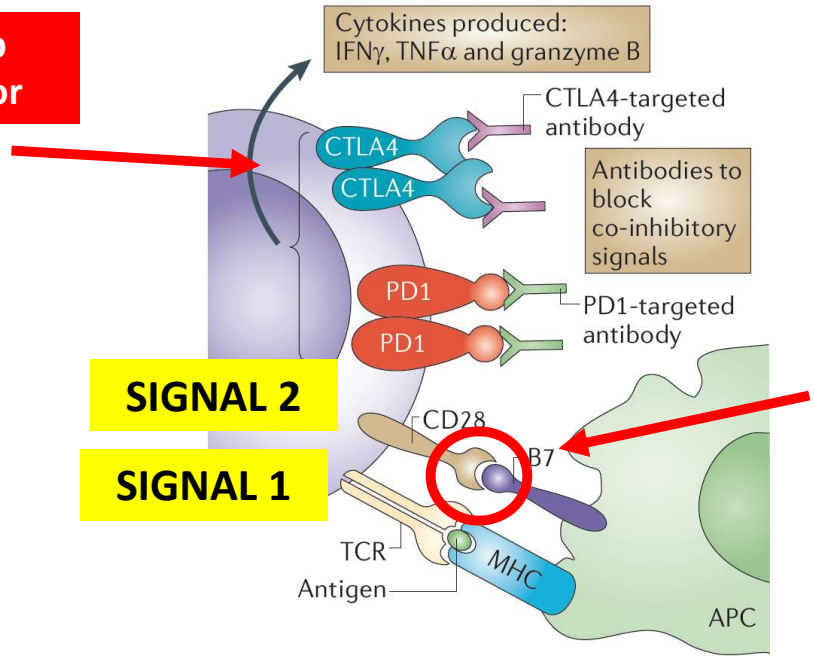
Sex and anti-inflammatory treatment affect outcome of melanoma and non-small cell lung cancer patients with rheumatic immune-related adverse events

Karolina Gente ,[1] Leonore Diekmann,[1] Lea Daniello,[2,3] Julia Will,[1] Manuel Feisst,[4] Victor Olsavszky,[5] Janine Günther,[1] Hanns-Martin Lorenz,[1] M Margarida Souto-Carneiro,[1] Jessica C Hassel ,[6] Petros Christopoulos,[2,3] Jan Leipe[7]

Gente K, et al. 2023. J Immunother Cancer.

Target CD80/86 overstimulation

Ruxolitinib
JAK Inhibitor



SIGNAL 2

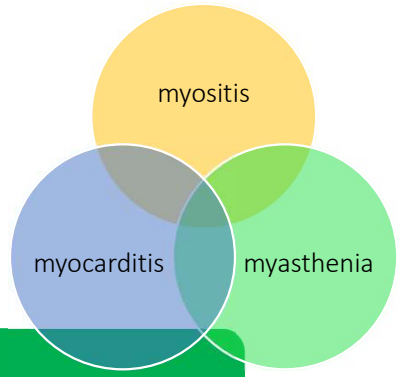
SIGNAL 1

Abatacept
CTLA4 agonist

CD, cluster of differentiation; CTLA4, cytotoxic T-lymphocyte associated protein 4; JAK, Janus kinase.

Image adapted from: Sharma P, et al. 2011. Nat Rev Cancer.

Abatacept/ruxolitinib and screening for concomitant respiratory muscle failure to mitigate fatality of immune-checkpoint inhibitor myocarditis



Suspected ICI-Myocarditis prospectively included (n=69)

n=27 excluded for ICI-myocarditis
n= 2 refused diagnosis work-up and care

75% anti-PD1 mono
25% combi + anti-CTLA4

Definite ICI-myocarditis (n=40)
Severity grading (G) criteria detailed in Supp-Table-5 (severe if G≥3)

74% cMRI
75% cardiac biopsy

Per chronological admission period

first 10 pts: using recommended guidelines

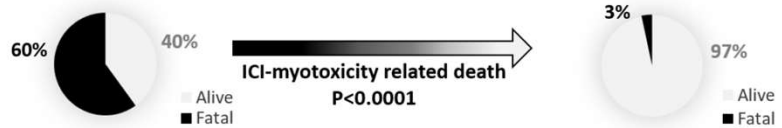
pulse IVMP ≥500 mg

expert consensus guidelines

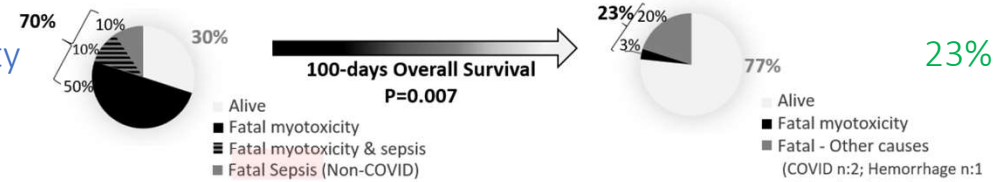
mechanism based approach

next 30 pts:
- systematic respiratory muscle involvement screening (ABG)
- active ventilation
- **ruxolitinib**
- **abatacept** with dose monitoring

1st quartile (05/2018-03/2020)	Start of:	Quartile 2-4 (03/2020-08/2021)
G1-2 (n=2), G≥3 (n=8)	- Prompt high dose abatacept (immune-monitored) & ruxolitinib (vs. mycophenolate) for G≥3 - Stop of plasmapheresis - Screening & ventilation of respiratory muscle failure	**G1-2 (n=8), G≥3 (n=22)**
Corticosteroids (n=10)		**Corticosteroids (n=26)**
Plasmapheresis (n=8)		**Abatacept (n=22)**
Abatacept (n=7)		**Ruxolitinib (n=18)**
Mycophenolate (n=4)		**Plasmapheresis (n=2)**
Tacrolimus (n=1)		IV immunoglobulin (n=5)*
IV immunoglobulin (n=2)*		Mycophenolate (n=2)*



70% mortality

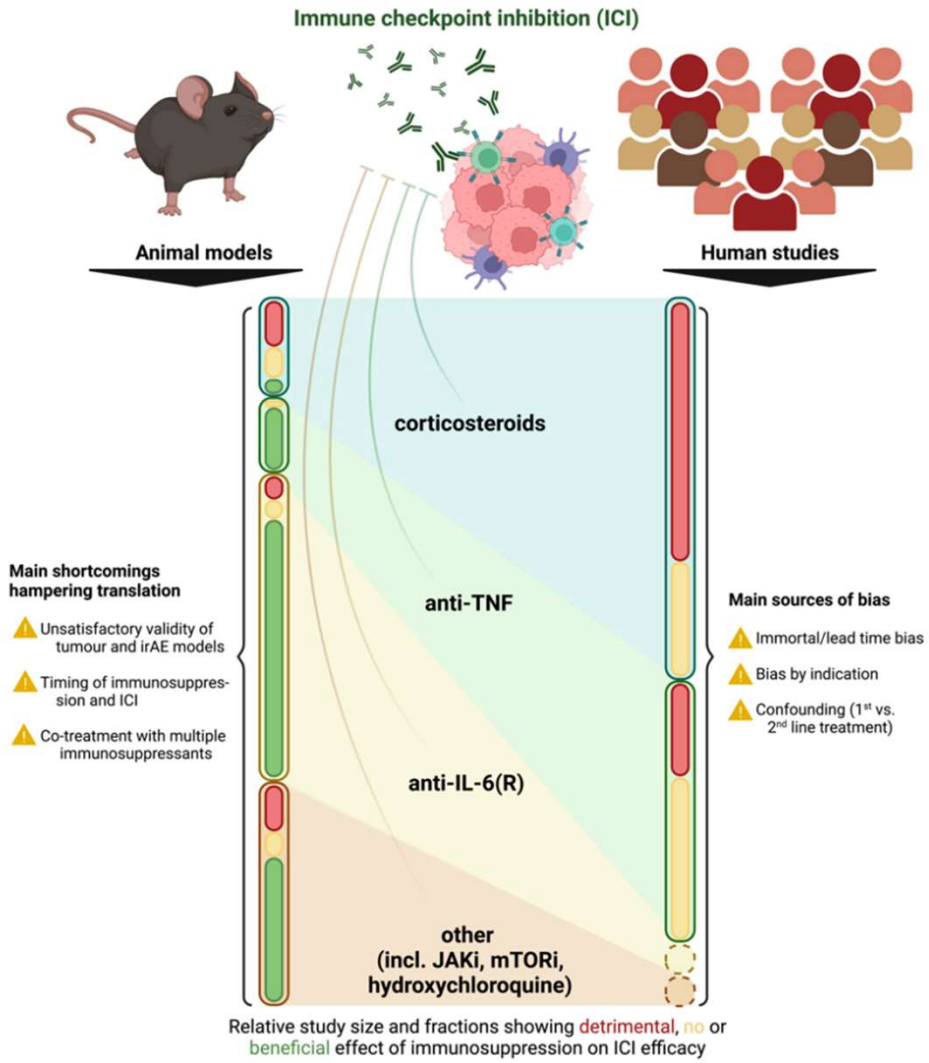


23% mortality

82% SD or PR
median PFS 5,7m

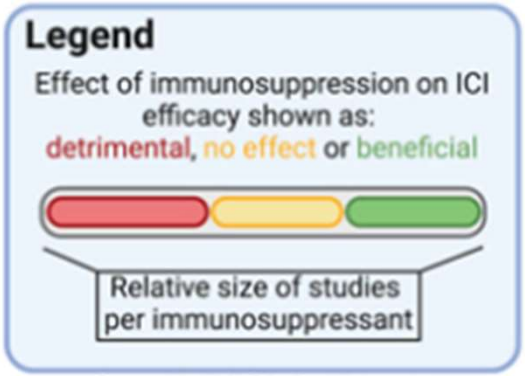
*Started before admission in our unit & transferred for poor evolution on these drugs (5/7 for IV immunoglobulin & 2/2 for mycophenolate). They were stopped upon admission in our unit. ABG, arterial blood gas; cMRI, cardiac magnetic resonance imaging; CTLA4, cytotoxic T-lymphocyte associated protein 4; G, grading; ICI, immune checkpoint inhibitor; IV, intravenous; IVMP, intravenous methylprednisolone; PD1, programmed death 1; pts, patients; PFS, progression-free survival; PR, partial response; SD, stable disease.

Salem JE, et al. 2023. Cancer Discov.
Image adapted from: Sharma P, et al. 2011. Nat Rev Cancer.



Clinical recommendations

- Be aware of possible detrimental effects of high dose corticosteroids and second-line immuno-suppression on ICI efficacy.
- Tailor immunosuppressants for irAEs to minimise detrimental effects on ICI efficacy.
- Consider vedolizumab as alternative for infliximab in ICI colitis.

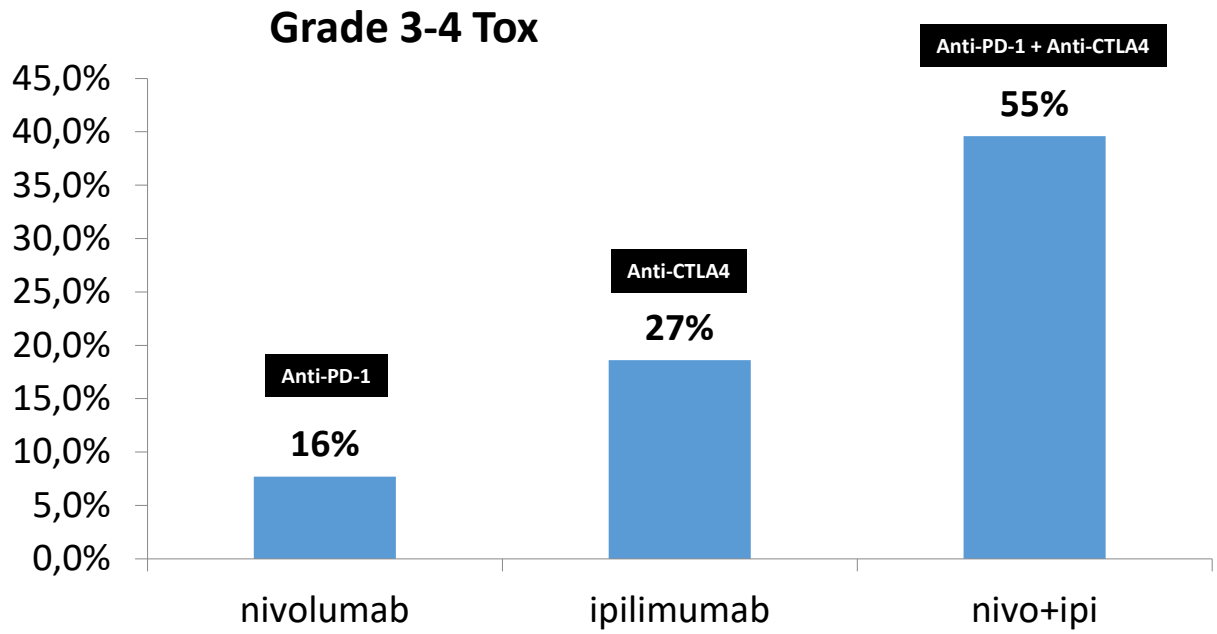


Created with BioRender.com

ICI, immune checkpoint inhibitor; IL-6(R), interleukin-6(receptor); irAE, immune-related adverse event; JAKi, Janus kinase inhibitor; mTORi, mammalian target of rapamycin inhibitor; TNF, tumor necrosis factor.

Verheijden RJ, et al. 2023. NPJ Precis Oncol.

The more combinations, the more toxicity?



CTLA4, cytotoxic T-lymphocyte associated protein 4; ipi, ipilimumab; nivo, nivolumab; PD-1, programmed death-1; Tox, toxicity.

Larkin J et al. N Engl J Med 2015;373:23–34.

Combination anti-CTLA4 + anti-PD(L)1

- Cave hypophysitis/colitis
- Minor suspicion of irAE: explore (lab tests, natural evolution)
- Toxicity tends to be more severe compared to monotherapy anti-PD1
  - FU on your patient (phone consult in between)
- Combine only if required: implicate patient in risk assessment
  - Melanoma: brain mets
- If irAE: stop both ICI
  - restart monotherapy only after resolution of irAE and no immunosuppression
  - Perform imaging before restart (if complete response: wait)
- ~~Dose dependency: melanoma: discuss ipi 1mg vs 3mg~~

CTLA4, cytotoxic T-lymphocyte associated protein 4; FU, follow-up; ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; mets, metastases; PD1, programmed death 1.

Combination anti-VEGF + ICI

- If required stop both ICI and anti-VEGF
- Restart TKI if quick resolution of symptoms
- If no resolution within 72h, discuss hospitalisation to explore
- Dose adaptation of TKI if necessary
- Restart IO
  - after resolution of irAE and no immunosuppression
  - Perform imaging before restart of IO (if complete response: wait)

BSMO immunomanager

BSMO, Belgian Society of Medical Oncology; ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; IO, immuno-oncology; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor.

BSMO immunomanager

Recommendations

Axitinib + anti-PD-(L)1

- Fatigue, hepatitis, diarrhea and hypothyroidism are AE that could be induced by both TKI and ICPI
- Grade II-III-IV toxicity: stop Axitinib: symptoms should regress within 72 hours
- Restart Axitinib in dose and timing according to usual recommendations

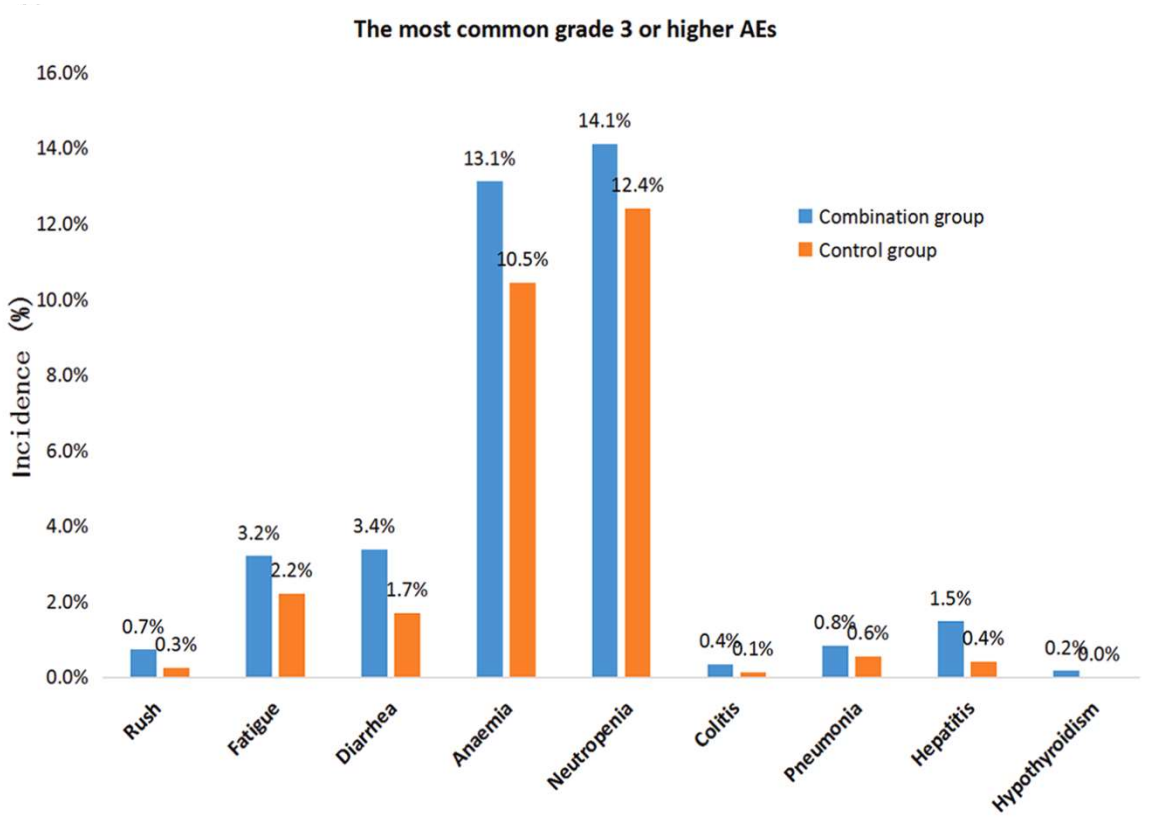
Warning signs for immune-related Adverse Events: these should be treated as such (overview immunomanager)

- **Rapid deterioration of one single AE**
- **Fever**
- **>1 suspected immune-related AE**
- **High CRP (which cannot be explained by other causes)**
- **Symptoms that do not regress within 72h of stop of Axitinib**

AE, adverse event; BSMO, Belgian Society of Medical Oncology; CRP, c-reactive protein; ICPI, immune checkpoint inhibitor; PD-(L)1, programmed death-(ligand)1; TKI, tyrosine kinase inhibitor.

https://www.bsmo.be/immunomanager/axitinib-anti-pdl/

Chemotherapy + ICI
Slightly more hemato toxicity



AE, adverse event; ICI, immune checkpoint inhibitor.

Mo DC, et al. 2021. Int Immunopharmacol.

Can we predict irAE?

Tumor

- Neoadjuvant vs metastatic setting with high tumor burden (Verheijden R et al, ESMO open 2020)

Patient

- Genetics
  - IL7 R variant
  - TCR beta variable gene polymorphism (Stephen B, et al. 2023. JITC)
- General characteristics
  - BMI (McQuade JL, et al. 2023. JAMA Oncol)
  - **Microbiome** (Dubin et al, 2016, Nat Comm)
- Underlying AID tendency
  - Pre-existing AID (Danlos FX, et al. 2018. EJC; Sternberg CN, et al. 2019. Eur Urol. [SAUL trial], Loriot Y, et al. 2020. EJC)
  - Kinetics of anti-TPO antibodies (Music M, et al. 2020. F1000Res)
- Serum biomarkers
  - Baseline TNFα (Weber J, et al. 2021. ESMO)
  - Baseline lower CD8 T_{CM}: predictive for arthritis (Bukhari S, et al. 2023. Cell Rep Med)
  - Baseline more CD4 T_{H2} cells: predictive for pneumonitis (Bukhari S, et al. 2023. Cell Rep Med)
  - Baseline more CD4 T_{H17} cells: predictive for thyroiditis (Bukhari S, et al. 2023. Cell Rep Med)

Therapy characteristics

- Baseline antibiotics (Jing Y, et al. 2022. JITC)
- Dose of anti-CTLA4

AID, autoimmune disease; BMI, body mass index; CD, cluster of differentiation; CTLA4, cytotoxic T-lymphocyte associated protein 4; ESMO, European Society for Medical Oncology; IL, interleukin; irAE, immune-related adverse event; T_{CM}, central memory T; TCR, T-cell receptor; T_H, T helper; TNF, tumor necrosis factor; TPO, thyroid peroxidase.

FORX

IL7 genetic variation and toxicity to immune checkpoint blockade in patients with melanoma

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Check for updates

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Taylor CA, at al. 2022;28(12):2592-2600.

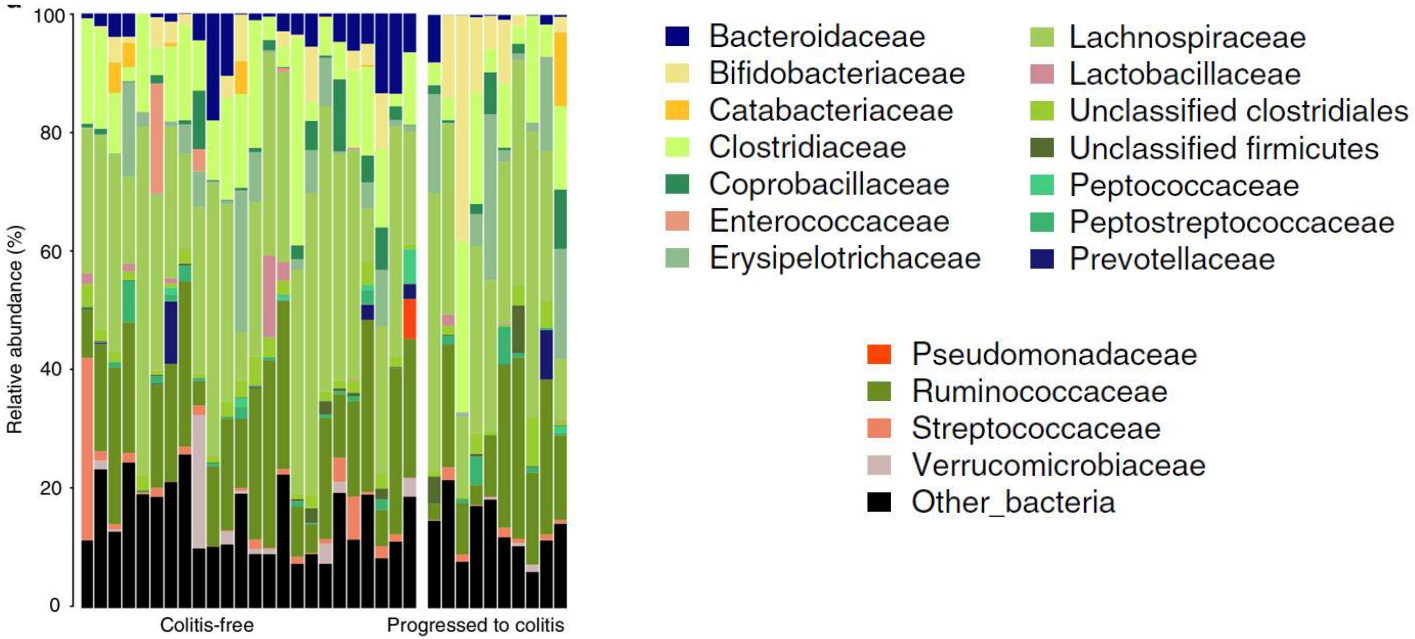
biomarkers

T-cell receptor beta variable gene polymorphism predicts immune-related adverse events during checkpoint blockade immunotherapy

Bettzy Stephen,[1] Joud Hajjar,[2] Shrutii Sarda,[3] Dzifa Yawa Duose,[4] Jeffrey M Conroy,[5] Carl Morrison,[6] Anas Alshawa,[1] Mingxuan Xu,[1] Abdulrazzak Zarifa,[1] Sapna P Patel ,[7] Ying Yuan,[8] Evan Kwiatkowski,[8] Linghua Wang,[9] Jordi Rodon Ahnert,[1] Siqing Fu,[1] Funda Meric-Bernstam,[1] Geoffrey M Lowman ,[3] Timothy Looney,[10] Aung Naing [1]

Stephen B, et al. 2023. J Immunother Cancer.

Microbiota and toxicity



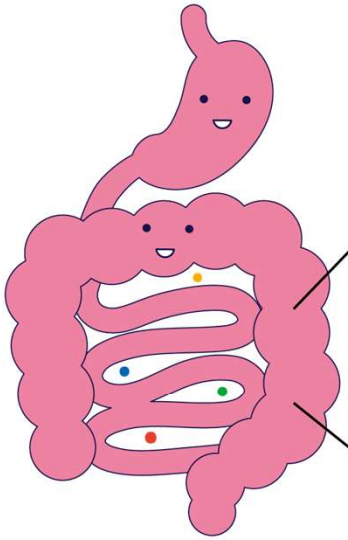
Dubin K, et al. 2016. Nat Commun.

FORX

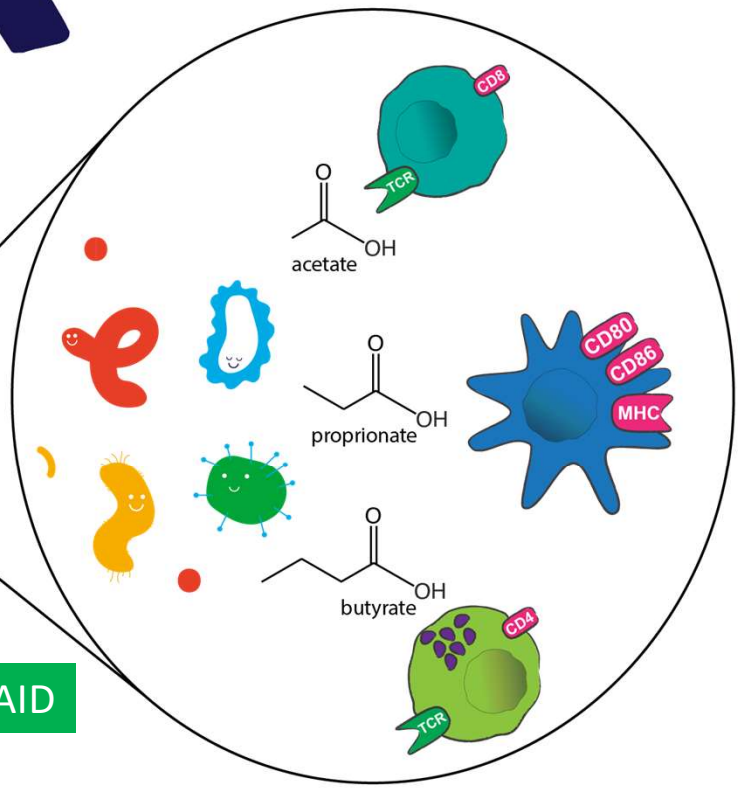
Diverse & lots of fibers

Better outcome ICI

More happiness

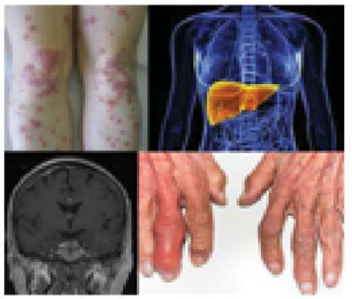


Less flares of AID



Less cardiovascular events

DIMINISH



Bolte LA, et al. 2023. Jama Oncol.
Larsen OFA. 2023. Front Nutr.
Berding K, et al. 2023. Mol Psychiatry.
McDonald D, et al. 2018. mSystems. Spencer CN, et al. 2021. Science.

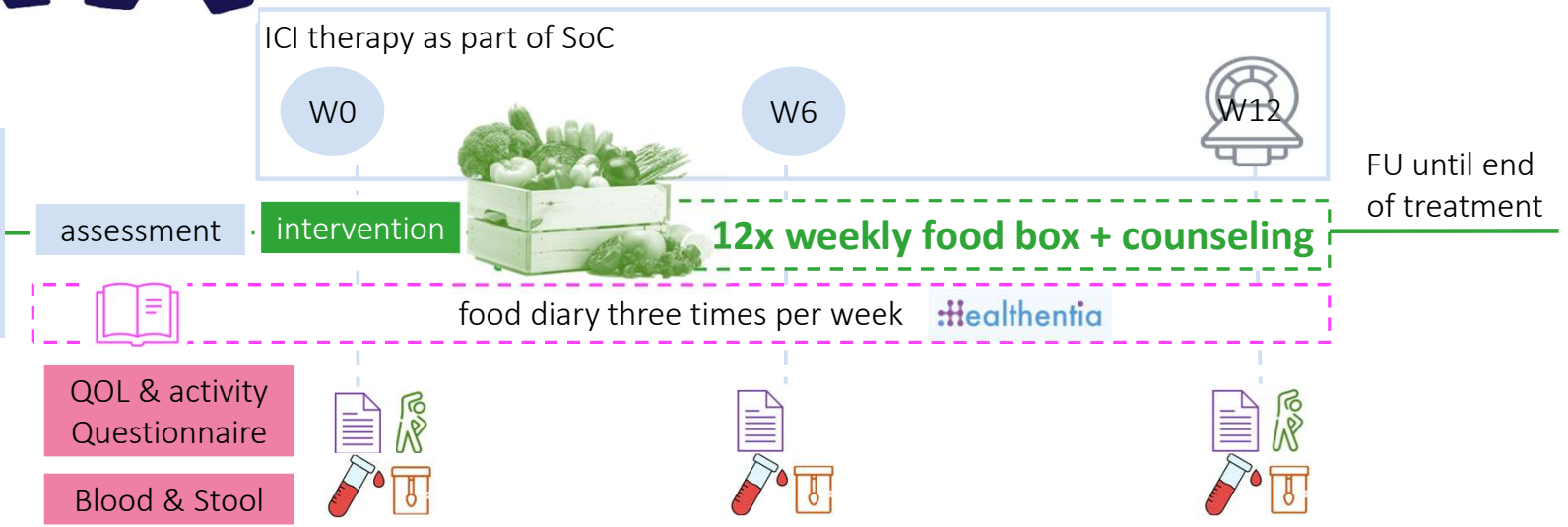
AID, autoimmune disease; FORX, FOod interventions to Reduce immunotoxicity; ICI, immune checkpoint inhibitor.

FORX

FOod interventions to Reduce immunotoXicity

20% reduction of irAE incidence

60 solid tumor pts starting anti-PD(L)1 +/- anti-CTLA4



CTLA4, cytotoxic T-lymphocyte associated protein 4; FORX, FOod interventions to Reduce immunotoxicity; FU, follow-up; irAE, immune-related adverse event; PD(L)1, programmed death (ligand)1; pts, patients; QOL, quality of life; W, week.

Verhaert M et al, ESMO 2023 (poster)

Oncologisch Centrum
Behandeling en Onderzoek van Kanker

VUB BISI BIOSTATISTICS & MEDICAL INFORMATICS RESEARCH GROUP

LMMO LABORATORY FOR MEDICAL & MOLECULAR ONCOLOGY RESEARCH GROUP

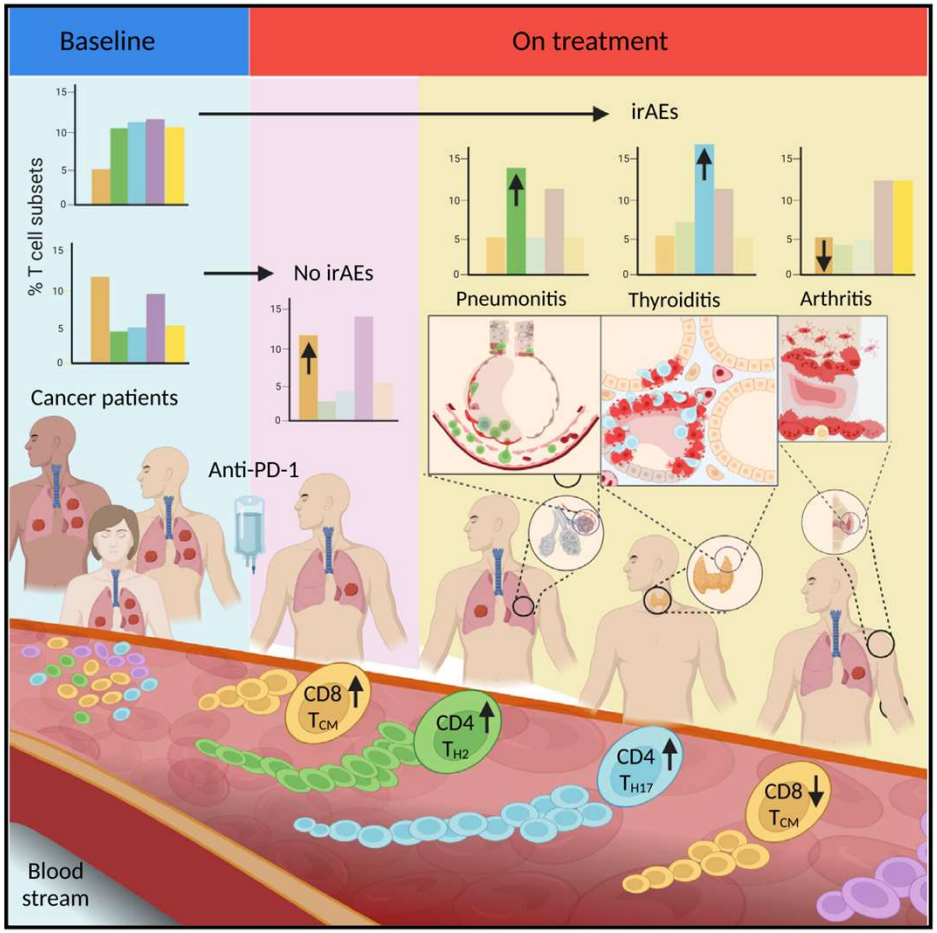
fwo

Can we predict irAE?
Higher dose = more irAE?

- Currently no evidence for anti-PD(L)1
- For anti-CTLA4:
  - Melanoma: ipi 3mg (q3w)/nivo 1mg: G3/4 AE: 59% (Wolchok JD, et al. 2017. NEJM)
  - Prostate Cancer: ipi 3mg (q3w)/nivo 1mg: G3/4 AE: 53% (Sharma P, et al. 2021. Cancer Cell)
  - Renal Cell Carcinoma: ipi 1mg (q3w)/nivo 3mg: G3/4 AE: 46% (Motzer RJ, et al. 2018. NEJM)
  - NSCLC: ipi 1mg (q6w)/nivo 3mg: G3/4 AE: 33% (Hellmann MD, et al. 2019. NEJM)
  - Melanoma: ipi 1mg(q3w)/nivo 3mg: G3/4 AE 34% (Lebbé C, et al. 2019. JCO. [Checkmate 511])
  - ColonCA MSI high: ipi 1mg (q6w)/nivo 3mg: G3/4 AE: 19% (Checkmate 142)

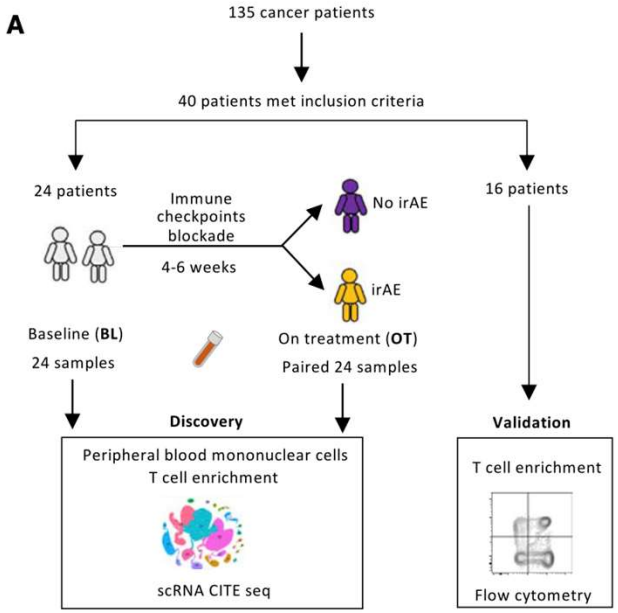
CTLA4, cytotoxic T-lymphocyte associated protein 4; G, grade; ipi, ipilimumab; irAE, immune-related adverse event; MSI, microsatellite instability; nivo, nivolumab; PD(L)1, programmed death (ligand)1; q3w, every 3 weeks; q6w, every 6 weeks.

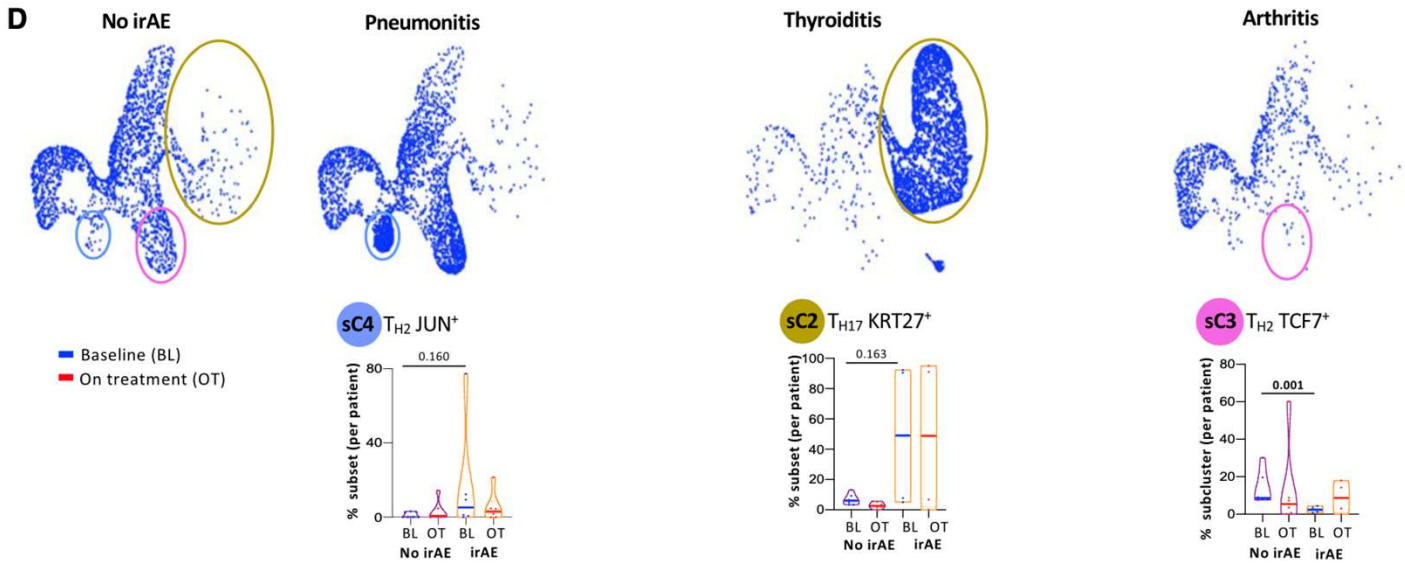
Can we predict irAE?



(Bukhari S, et al. 2023. Cell Rep Med)

Can we predict irAE: we will!





Baseline blood sample
-lower CD8 TCM: predictive for arthritis
-more CD4 TH2 cells: predictive for pneumonitis
-more CD4 TH17 cells: predictive for thyroiditis

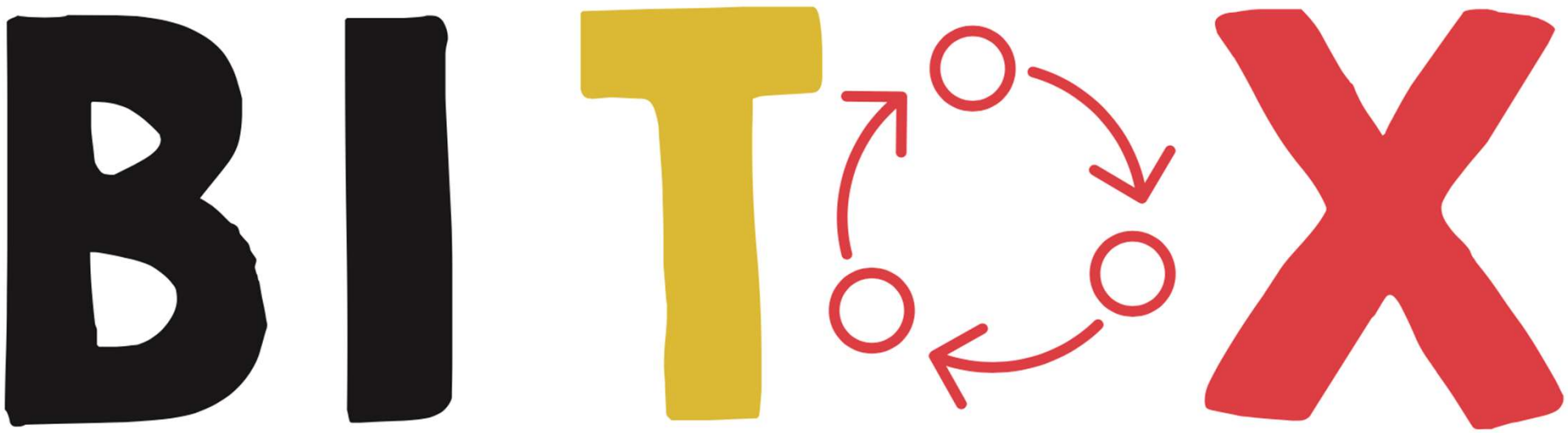
(Bukhari S, et al. 2023. Cell Rep Med)

Which markers which indicate severity/chronicity of irAE? → implications for anti-irAE therapy: corticoids or not?/2nd line IS or not?) continuation ICI (esp if adjuvant setting, CR)

- Hepatitis
  - Bilirubine alteration (De Martin E, et al. 2018. J Hepatol)
  - Liver comorbidities/general symptoms (encephalopathy a.o.) (Alouani E, et al. 2023. Eur J Cancer)
  - IL1beta (Zeng L, et al. 2023. Lung Cancer)
- CRP: worse tumor outcome (Lauwyck J, et al. 2021. Melanoma Research)
- irAE or paraneoplastic syndrome? (beware of anti-Hu encephalitis)

- More research needed!
  - Age?
  - Dysbiosis?
  - Underlying AID? (Gente K, et al. J Immunother Cancer. 2023;11(9):e007557: worse OS for AID flare vs irAE)
  - Which paraneoplastic syndromes?

AID, autoimmune disease; CR, complete response; CRP, c-reactive protein; ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; IS, immunosuppressant; OS, overall survival.


BITX

We started in march 2021 BITOX a successful network to tackle irAEs in Belgium

BITOX

BITOX

Belgian Multidisciplinary Immunotoxicity Board

founded by Sandrine Aspeslagh in March 2021, organised by Sandrine and Marthe Verhaert

bi-monthly virtual meeting between oncologists (70%) and organ specialists (30%)

goals: discuss complex immunotherapy cases to gather knowledge and experience about irAEs in order to obtain consenus about their management

every 1st and 3rd Monday of each month 17:00 - 18:00

CASES

37% dysimmunity cases

63% irAE cases

types of toxicity

joint, pneumological, muscle, cardial, endocrinological, hepatic, digestive, neurological, eye, other

types of dysimmunity

underlying autoimmune disease
transplantpatient
ongoing corticoid treatment
ongoing antibiotics
paraneoplastic syndrome
ECOG >2
previous irAE
other

top 3 types of cancer

melanoma
NSCLC
RCC

BITOX

NETWORK

doctors from:

Flanders
55,4%

Brussels
34,4%

Wallonia
10,2%

hospitals
that contacted us:

42,5% university hospitals
57,5% peripheral hospitals

about 41
organ specialists
helped us:

spread over 10 groups
2-6 per organ specialty

MEETING

173
invites per meeting

on average
4
cases per meeting
(between 1 and 6)

spoken language:

English

but Dutch and French
are also possible
(certainly when signing up!)

cases are submitted
online or via mail

Severe and complex irAE

Anti-CTLA4

IMJUDO®

YERVOY™

OPDIVO™

BAVENCIO® avelumab Injection 20 mg/mL

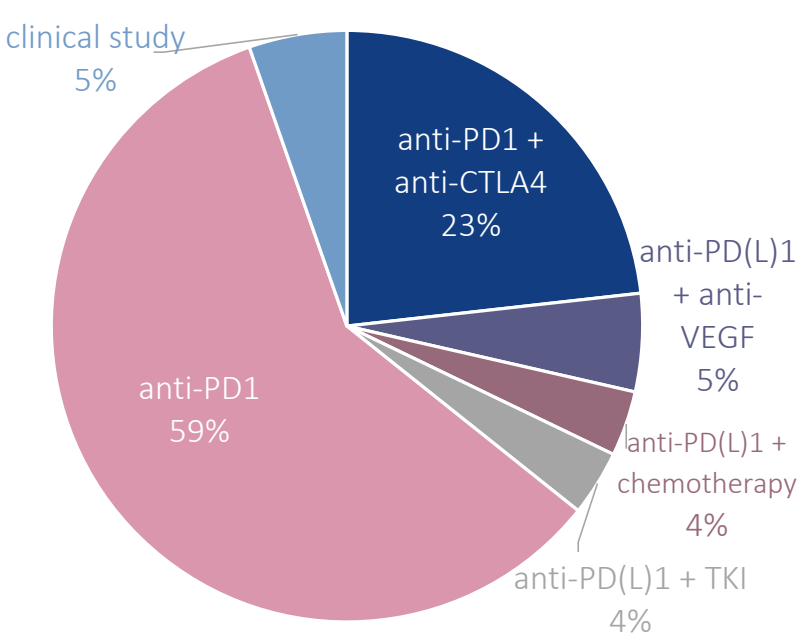
IMFINZI™

KEYTRUDA®

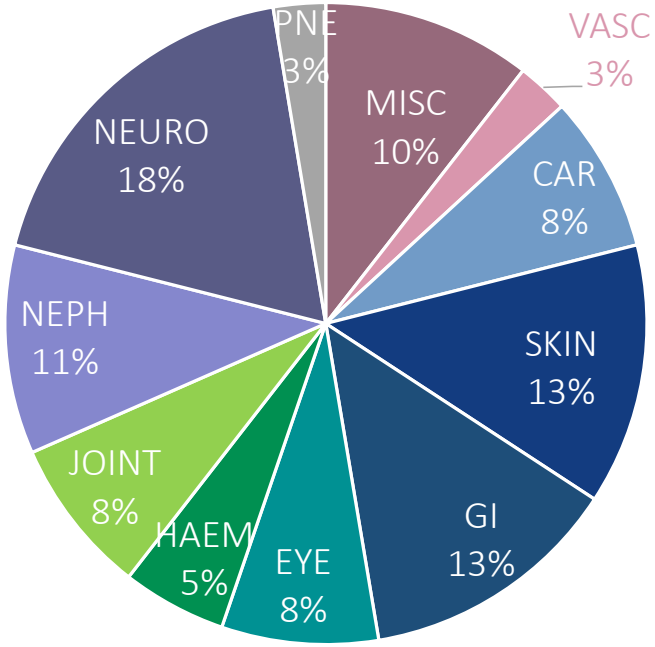
TECENTRIQ®

LIBTAYO® (cemiplimab-rwlc)

Anti-PD1



type of immunotherapy



type of toxicity

CTLA4, cytotoxic T-lymphocyte associated protein 4; irAE, immune-related adverse event; PD1, programmed death 1.

Acknowledgements

BITOX

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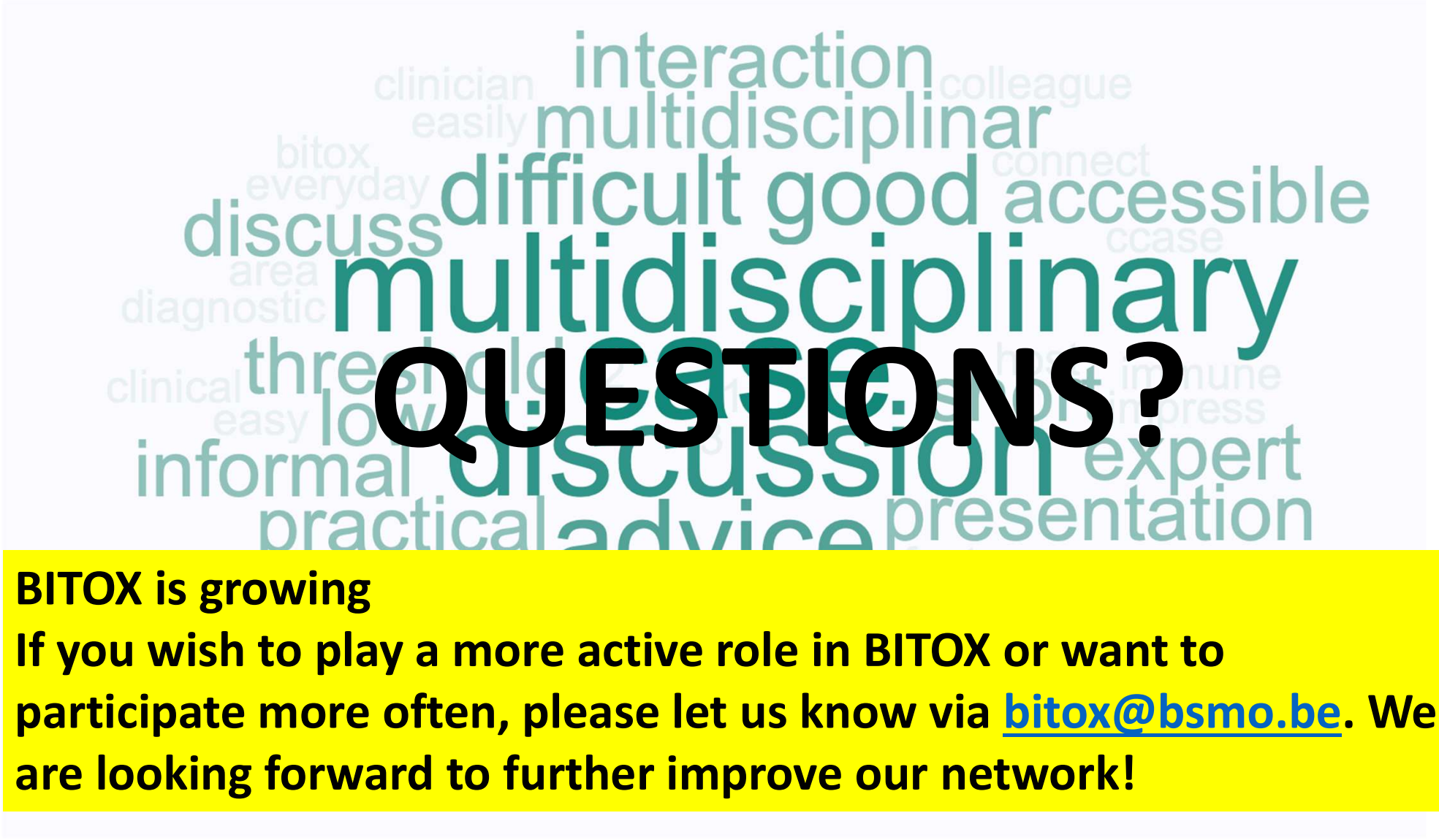

BITOX is growing

If you wish to play a more active role in BITOX or want to participate more often, please let us know via bitox@bsmo.be. We are looking forward to further improve our network!

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Enjoy the break

18.05-18.20	BREAK			
18.25	18.25 => 19.05 PLENARY 2 Novel concepts in cancer Immunotherapy B ROUTY T KERRE S RAUH (Mod)			
19.10		19.10=>19.50 Patient education: Examples from academics centers T KERRE S STREEL M VANDEVELDE J VANSTEENKISTE (Mod)	19.10=>19.50 CAR T vs Bispecifics : Toxicity and sequencing P VANDENBERGHE J CAERS R SCHOTS (Mod)	19.10=>19.50 Drug Interference during Immunotherapy M ILZKOVITZ B ROUTY A AWADA (Mod)
19.50	19.50 => 20.05 CLOSING P LACANTE & P COULIE			
20.00 - 22.00	WALKING DINNER			