ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

Workshop

Managing patients with underlying autoimmune diseases

Galatea, floor 2

Eric Van Cutsem, *UZ Leuven*

and

Olivier Malaise, *CHU Liege*

Moderated by

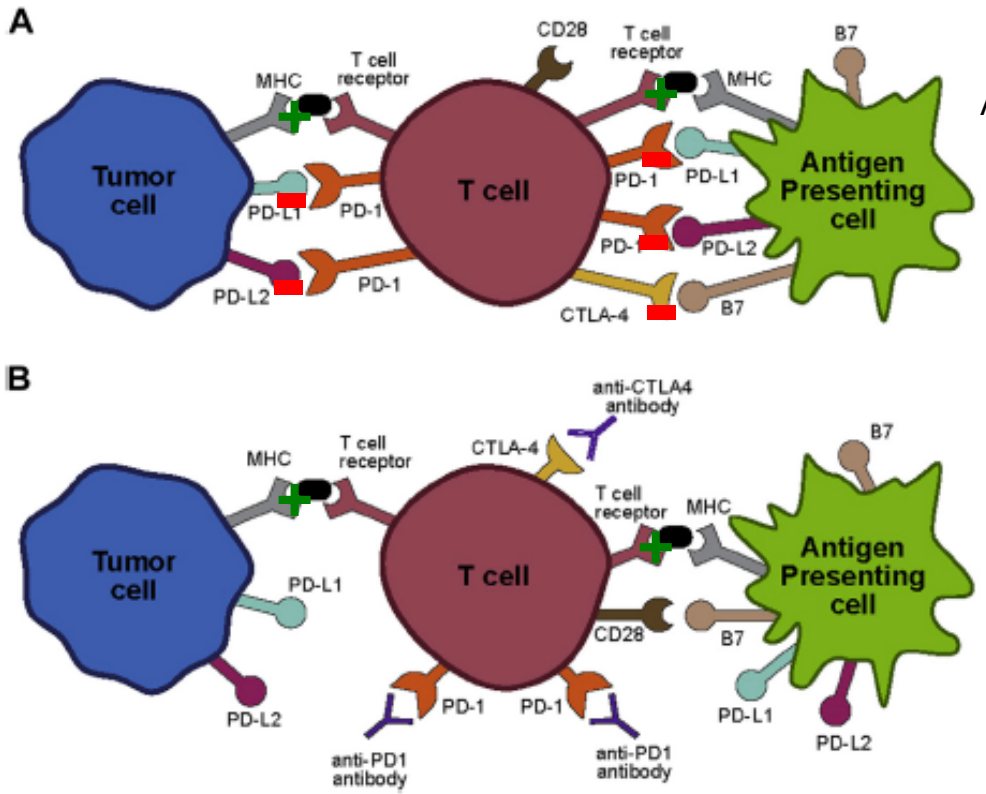
Bernard Lauwerys, *UCL*

Mercury number IOBE18NP04371-09

Date of preparation: December 2018

I want to introduce checkpoint inhibitor for my patient.
But he has a history of auto-immune disease.

What do I have to know ?



Adapted from Cappelli LC et al. 2017.

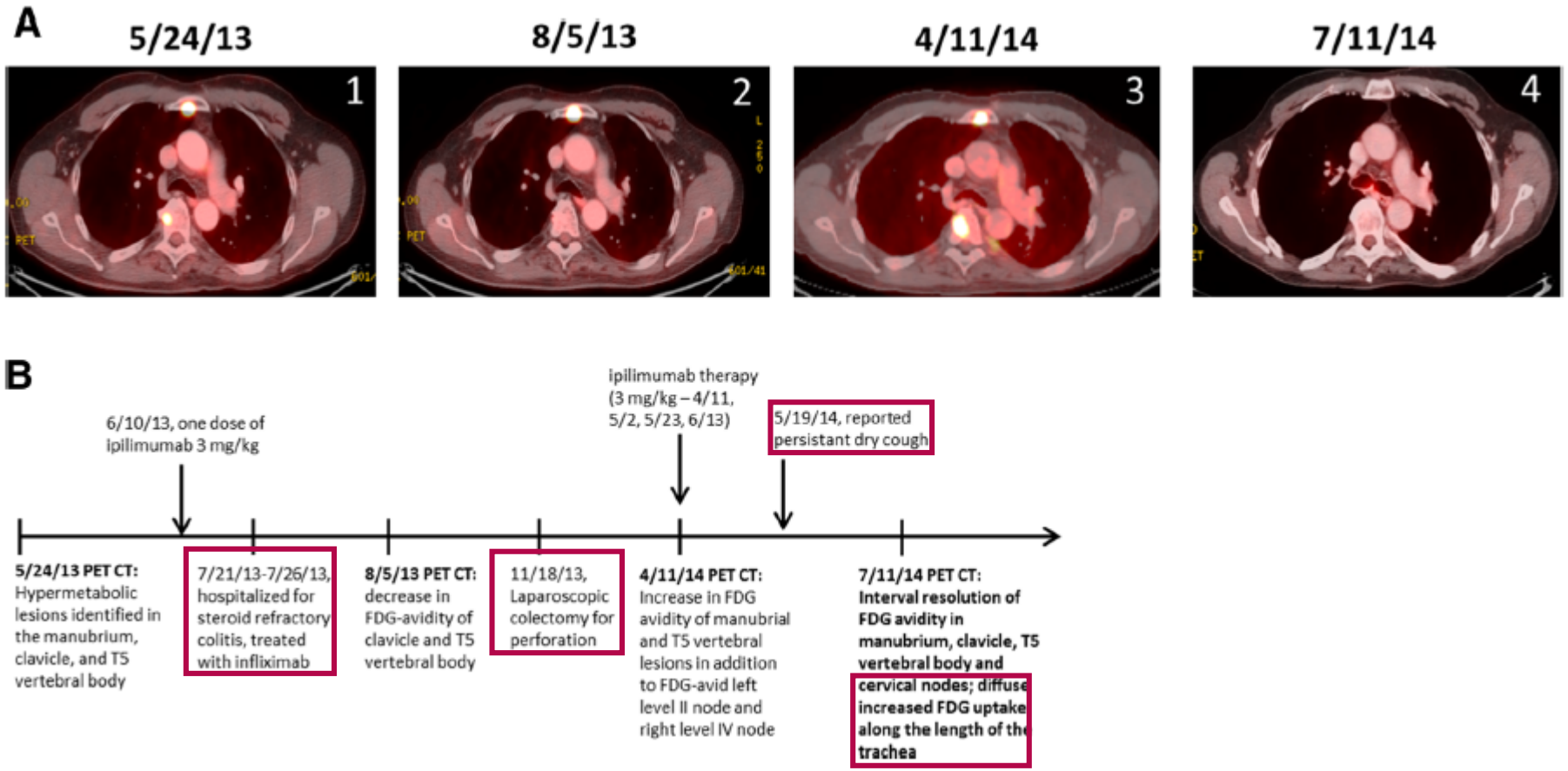
- USA: between 20–50 million people with an autoimmune disease[1]
- Autoimmune disease: excluded from the clinical trials
- Safety and efficacy were <u>poorly known</u>

MHC, major histocompatibility complex.

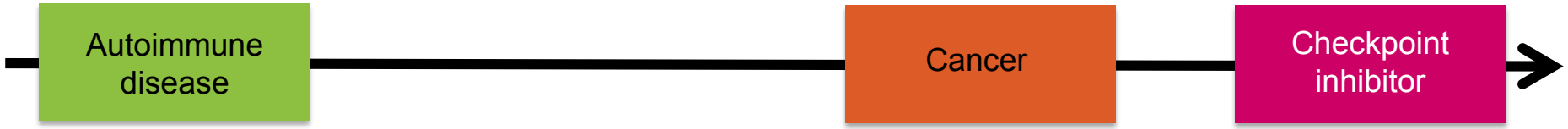
1. https://www.aarda.org/news-information/statistics/. Accessed December 2018. 2. Cappelli et al. Rheum Dis Clin N Am 2017;43:65–78.

Introductive clinical case (from literature):

61 year old male, with ulcerative colitis previously treated with TNF inhibitor and azathioprine



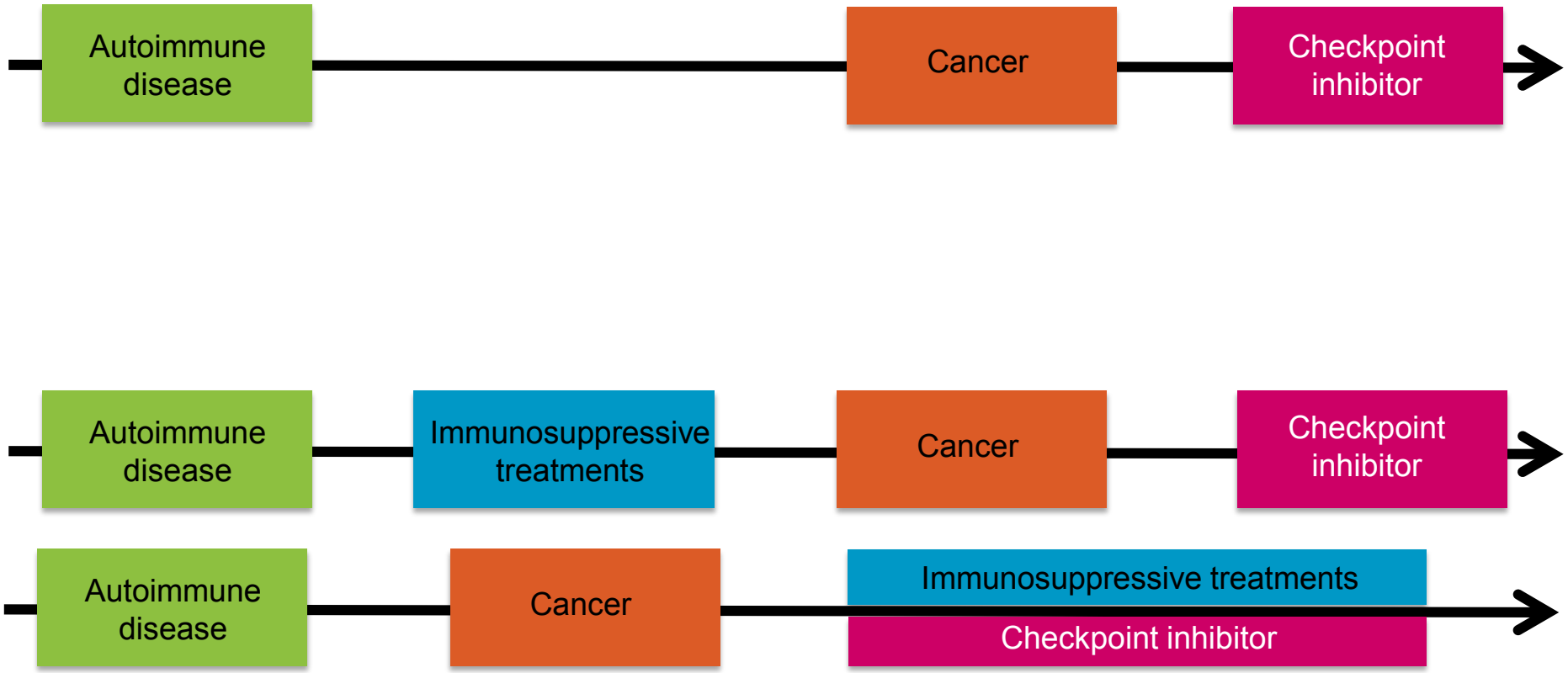
FDG, fludeoxyglucose; TNF, tumor necrosis factor.
Bostwick et al. J Immunother Cancer 2015;3:19.



Q1: Efficacy and safety of checkpoint inhibitor in patients with underlying autoimmune disease

Q2: Influence activity of baseline autoimmune disease on irAE

irAE, immune-related adverse event.

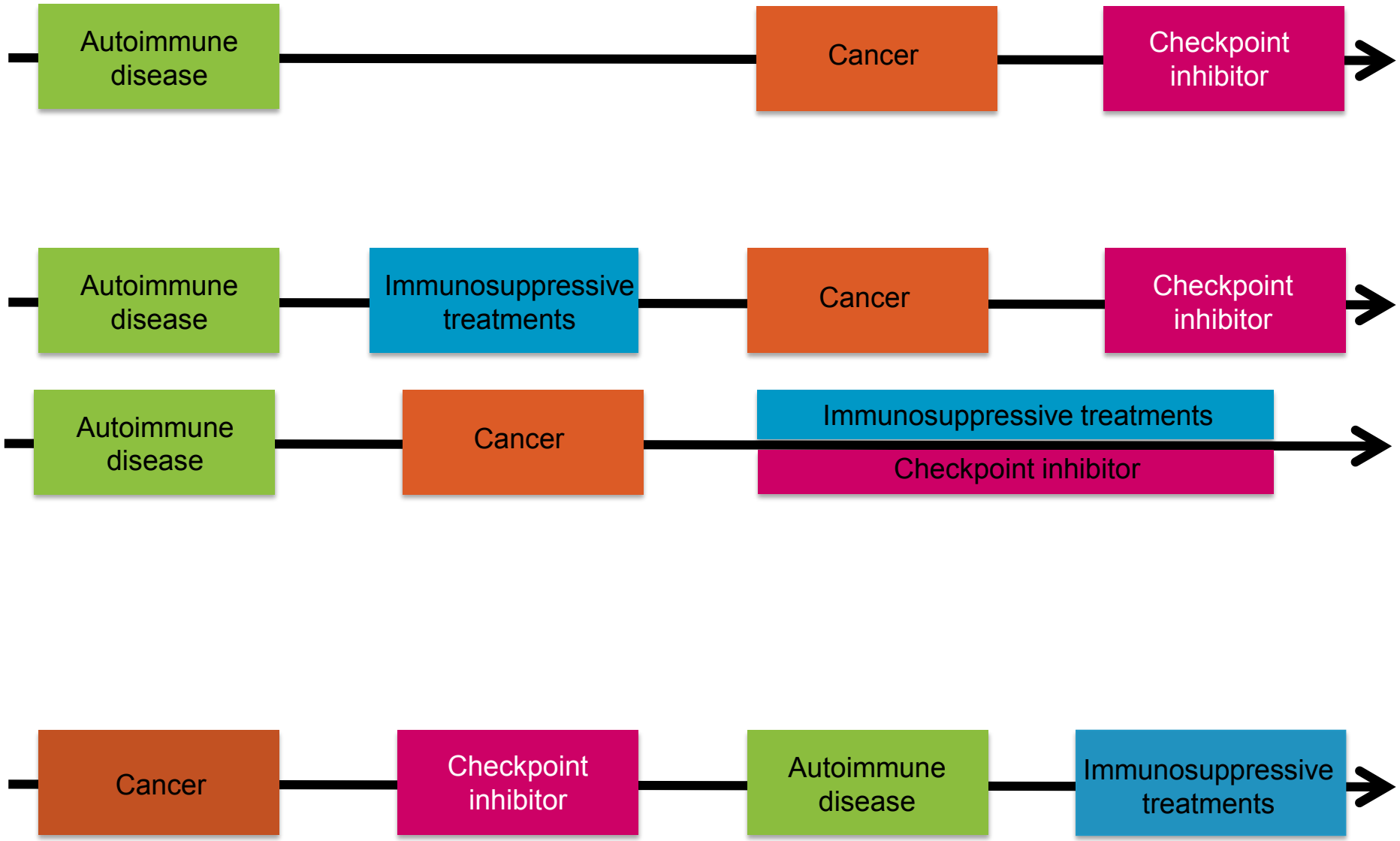


Q3:

* Influence of the immunosuppressive treatment (used to treat baseline autoimmune disease) on the CPI response?

* Influence of a concomitant immunosuppressive treatment on the CPI response?

CPI, checkpoint inhibitor.



Q4: Influence of the immunosuppressive treatment (used to treat the irAEs) on the CPI response?

Q1: Efficacy and safety of check-point inhibitor in patients with underlying autoimmune disease

56 patients NSCL under PD1 and PDL1

49%: rheumatologic base-line disease
18%: active disease
20%: under immunomodulatory baseline agent

Results:

Response (partial/complete): 22%
Disease control: 53%
No link with irAE apparition

Table 1. Autoimmune Disease Types Among 56 Patients With Non–Small-Cell Lung Cancer

Autoimmune Disease	Patients (n = 56)
Rheumatologic	25 (45)
Rheumatoid arthritis[a,b,c]	11
Polymyalgia rheumatica[c,d]	5
Seronegative arthritis	4
Scleroderma	2
Psoriatic arthritis[d,e]	2
Systemic lupus erythematosus	1
Sjögren syndrome	1
Temporal arteritis	1
Dermatologic	16 (29)
Psoriasis[a,b,d,e,f]	14
Alopecia areata	1
Discoid lupus	1
Endocrine	9 (16)
Graves thyroiditis[f]	5
Hashimoto thyroiditis	4
Gastrointestinal	6 (11)
Ulcerative colitis[g]	3
Crohn disease	3
Neurologic	3 (5)
Myasthenia gravis	1
Multiple sclerosis[g]	2
Others	3 (5)
Rheumatic fever	2
Autoimmune hemolytic anemia	1

NOTE. Data are reported as No. or No. (%). Patients who had more than one autoimmune disease are indicated with a repeated superscript letter.

NSCL, non-small cell lung cancer.
Leonardi et al. J Clin Oncol 2018;36:1905–12.

Q1: Efficacy and safety of checkpoint inhibitor in patients with underlying autoimmune disease

56 patients NSCL under PD1 and PDL1

Disease flare-up and/or irAE: 55%

Disease flare-up: 23%
Usually mild, CPI stopped only in 14%
No need for IS other than GC

More often disease flare-up occurs if:
* rheumatological baseline disease (40% vs 10%, p = 0.01)
- symptomatic baseline autoimmune disease (50%, vs 18% p = 0.04)
* under baseline IS or not? No

SAFE WITHOUT LIFE-THREATENING EVENTS AND WITHOUT EXCESS OF TREATMENT DISCONTINUATION

Table 5. Immune-Related Adverse Events

Characteristic	Patients
irAE unrelated to the underlying AID	
Patients who did not develop irAEs	35 (62)
Patients who developed irAEs*	21 (38)
irAEs experienced among 21 patients	23
Grade 1-2	17 (74)
Grade 3-4	6 (26)
Treatment required for irAEs†	
No treatment required	7
Supportive care‡	10
Systemic corticosteroids	7
PD-(L)1 inhibitor dosing during irAEs	
Continued	10
Temporarily discontinued	3
Permanently discontinued	8

NOTE. Data are reported as No. or No. (%).
Abbreviations: AID, autoimmune disease; irAE, immune-related adverse event; PD-(L)1, programmed death (PD) 1 or PD-ligand 1.
*Two of the 21 patients developed two different irAEs.
†Two of the 21 patients developed two irAEs, and one patient received both systemic corticosteroids and filgrastim (supportive care).
‡Patients received one of the following treatments: nonsteroidal anti-inflammatory drugs, loperamide, levothyroxine, desmopressin, or filgrastim.

AID, autoimmune disorder; GC, glucocorticoid; IS immunosuppressant.
Leonardi et al. J Clin Oncol 2018;36:1905–12.

Q1: Efficacy and safety of checkpoint inhibitor in patients with underlying autoimmune disease

52 patients with AID under anti-PD-1 advanced melanoma

AI disorder[a]		
Rheumatologic	27 (52%)	RA 13, sarcoidosis 3, PMR 3, SLE 2, scleroderma 2, psoriatic arthritis 2, Sjogren's 2
Dermatologic	8 (15%)	psoriasis 6, eczema, erythema nodosum
Gastrointestinal	6 (12%)	CD 3, UC with colectomy 2, celiac disease 1
Neurologic	5 (10%)	GBS 2, CIDP 1, MG 1, Bell's palsy 1
Endocrine	4 (8%)	Graves' disease 4
Respiratory	2 (4%)	Asthma 2 (1 severe on long-term oral steroids)
Hematologic	2 (4%)	ITP 2
Activity of AI disorder at PD1 start		
Not clinically active	37 (71%)	
Clinically active	15 (29%)	11 rheumatologic (RA 5, psoriatic arthritis 2, Sjogrens 2, sarcoidosis 1, PMR 1), 3 psoriasis, 1 severe asthma

- More often recurrence of AID (38%) than new autoimmune manifestation (29%). Global rate of irAE of 50%
- More often if **active disease** (60 vs 30, p = 0.039), more often if **rheumatological disease** (because more active?)
- More often if **IS at baseline** (because more active disease?)
- Usually mild, 8 temporarily discontinued, 2 definitely stopped (10% of the flare-ups, only 4% of the total group)
- Response in 17/52 (33%), no difference of response if irAE or not

SAFE WITHOUT LIFE-THREATENING EVENTS AND WITHOUT EXCESS OF TREATMENT DISCONTINUATION

Menzies et al. Ann Oncol 2017;28:368–76.

Q1: Efficacy and safety of check-point inhibitor in patients with underlying autoimmune disease

52 patients with AID under anti-PD-1 advanced melanoma

Also: 67 patients with previous irAE under ipilimumab and experimented anti-PD-1

Previous irAE under ipilimumab :

Usually serious (86% with Grade 3 or 4)

Usually colitis (62 patients had a colitis Grade 3 or higher)

Therapeutic response in 40%

Recurrence of the irAE: only 3% (1 arthritis, 1 colitis)

New irAE: 34% (14 patients)

21%: Grade 3 or higher

8 (12% of the total group): stop immunotherapy (4 pneumonitis, 2 hepatitis, 1 colitis, 1 myasthenia)

SAFE TO INTRODUCE ANOTHER CPI

Menzies et al. Ann Oncol 2017;28:368–76

Q1: Efficacy and safety of check-point inhibitor in patients with underlying autoimmune disease

REVIEW

123 patients in 49 publications (including clinical case reports > selective bias is possible !)

- 46.2% had active disease
- 43.6% had concommitant treatments

75% had exacerbation of previous AI disease, irAE or both

- 41% exacerbation of the previous disease
- 31% irAE (mainly colitis and hypophysitis)
- 11% both

Overall, 50% of disease recurrence

If irAE, need for GC in 62% and other additionnal IS in 16%. The irAE improved in more than 90%.

17.1% (21 patients) of the patients definitively stopped CPI but reintroduced in 10 (only 2 other irAE)

4.1% (5 patients) of the patients died, 2 because of irAE

Abdel-Wahab N et al. Ann Intern Med 2018;168:2:121–130.

Q1: Efficacy and safety of check-point inhibitor in patients with underlying autoimmune disease

30 patients with AID under ipilimumab advanced melanoma

INCLUDED IN THE PREVIOUS REVIEW (Abdel-Wahab Annals of internal medicine 2018)

Disease flare-up: 27%
* All managed with GC alone

New irAE Grade ≥ 3: 33%
* Managed with GC and infliximab (1)

* 1 death: cutaneous psoriasis that developed a colitis

Patient No.	Baseline Condition	Autoimmune Exacerbation	Treatment	Immune-Related Adverse Event
2	Sarcoidosis	...	...	Glaucoma
3	RA	Joint pain	As for hypophysitis	Hypophysitis
4	RA	...	...	Thyroiditis
5	Psoriasis	Worsening plaques	As for colitis	Colitis
6	Psoriasis, Graves disease	...	...	Hypophysitis
8	RA, polymyalgia rheumatica	Joint pain, myalgias	Prednisone 30 mg/d tapered over 1 mo	...
9	RA	Joint pain	Prednisone 15 mg/d down to 10 mg	...
11	Transverse myelitis	...	...	Colitis
12	Crohn disease	...	...	Colitis
14	Ulcerative colitis	Diarrhea, disease flare	Infliximab, dexamethasone 2 mg daily[a]	...
15	Inflammatory arthritis[b]	Joint pain	As for colitis	Colitis
20	Psoriasis	...	...	Hypophysitis
23	Sarcoidosis	Hypercalcemia, renal insufficiency	Prednisone 25 mg/d, tapered to 20 mg after 4 wk	...
24	RA	Joint pain	Prednisone 10 mg/d, now receiving 8 mg/d	...
28	Psoriasis	...	...	Presumed colitis grade 5

Johnson DB et al. JAMA Oncol 2016;2:2:234–240.

Q1: Efficacy and safety of check-point inhibitor in patients with underlying autoimmune disease

19 patients with AID under ipilimumab advanced melanoma

INCLUDED IN THE PREVIOUS REVIEW (Abdel-Wahab, Annals of Internal Medicine 2018)

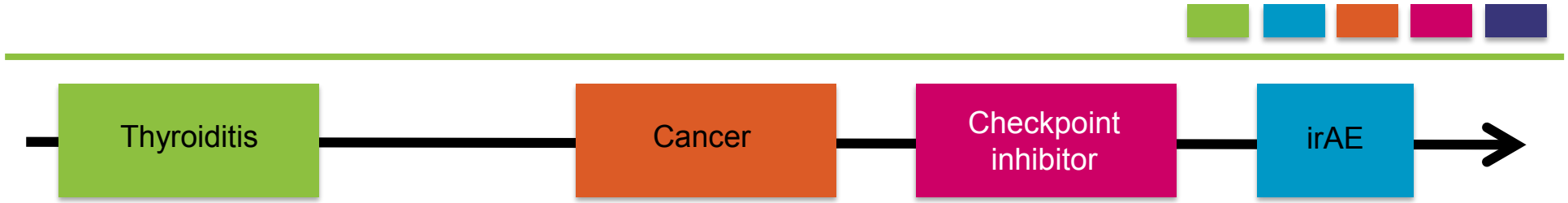
42%: flare-up of their AID (more often if rheumatological disease, 55%)
16%: new irAE

Response rate of 30%

Controlled with IS therapy (CS, but also IVIg for myositis). No disruption of immunotherapy

Gutzmer R et al. Eur J Cancer 2017;75:24–32.

Focus on thyroiditis and inflammatory bowel disease



Baseline thyroiditis n = 11

5 (45%) had adverse events

2 (17%) worsening

3 (27%) de novo new irAE : hypophysitis, hyperthyroidism, type 1 diabetes

2 patients had to stop the CPI therapy

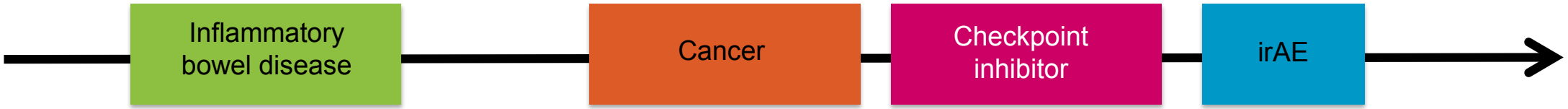
Baseline inflammatory bowel disease n = 13

8 (62%) had adverse events

5 flare-ups (39%) with **1 perforation** and **1 death** (because of concomitant cutaneous irAE)

5 patients were active: only 2 had an AEs > no influence of the baseline activity

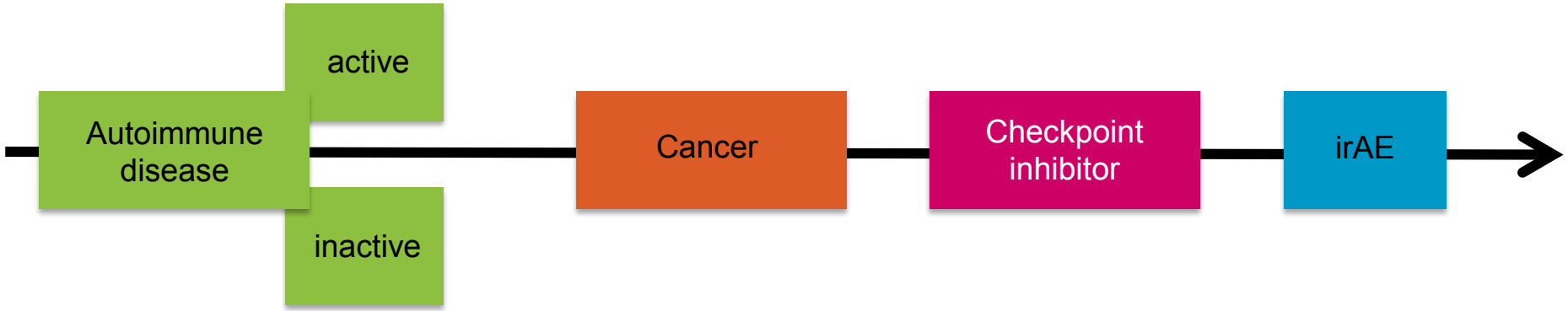
4 patients had to stop the CPI therapy



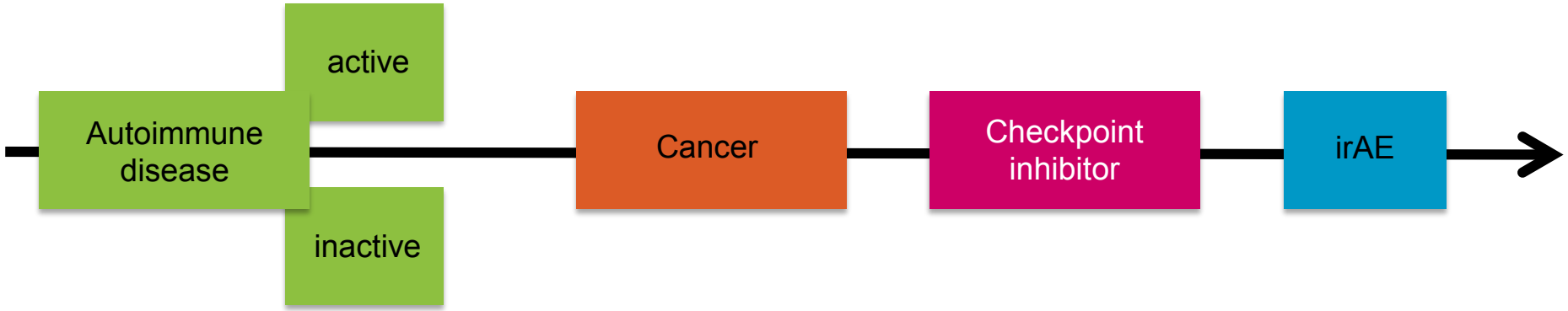
Intermediate conclusion

- Similar rate of new irAE, but risk of baseline disease flare-up in 1/3 or 1/2
  - Usually, flare-ups are mild with good response to GC
    - Same rate of response as in general population
      - No excessive treatment discontinuation
- No contraindication to give immunotherapy, but careful monitoring

Q2: Influence activity of baseline autoimmune disease on irAE?



Q2: Influence activity of baseline autoimmune disease on irAE?



2 studies available

(1) Menzie 2017 (n = 52): more irAE if active disease (60% vs 30%), p = 0.039

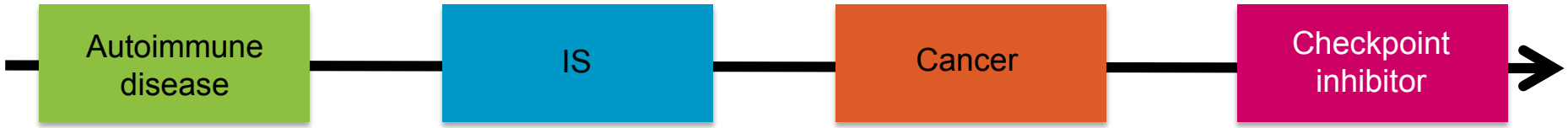
(2) Abdel-Wahab 2018 (review, n = 106): no differences (67% vs 75%), n.s.

- Baseline IS treatment: tendency to less irAE (59 vs 83%), n.s.

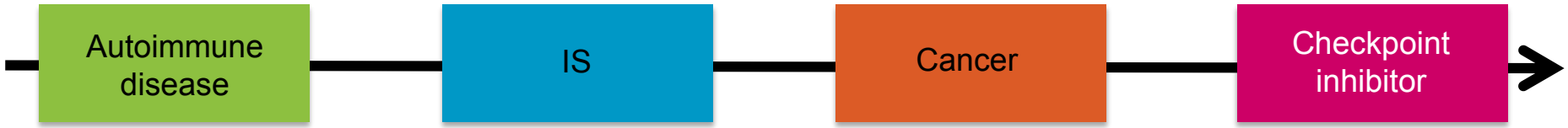
n.s., non-significant.

1. Menzies et al. Ann Oncol 2017;28:368–76. 2. Abdel-Wahab N et al. Ann Intern Med 2018;168:2:121–130.

Q3: Influence of the immunosuppressive treatment (used to treat baseline autoimmune disease) on the CPI response?



Q3: Influence of the immunosuppressive treatment (used to treat baseline autoimmune disease) on the CPI response?



* 19 patients (anti-PD-1)[1]

6 under IS at start of the treatment

2/6 (33%) patients with IS vs 4/13 (31%) showed a partial response : *n.s.*
For the 2 patients under IS with RA: sulfasalazine and prednisolone
1 patient under etanercept (anti-TNF) + MTX: no tumor response

* 56 patients: anti-PD(L)-1 and NSCLC

11 under IS at start of the treatment

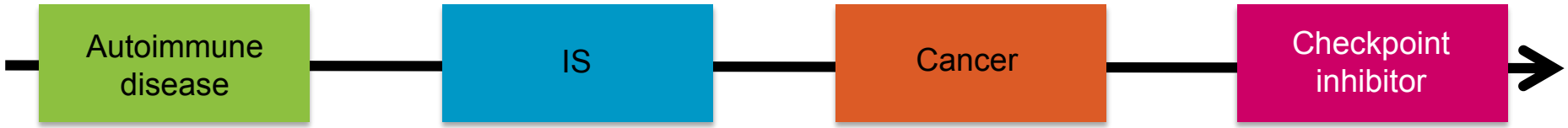
Topical steroid (1); prednisone (3); hydoxycholoroquine (2); sulfasalazine – salazopyrine (3); apremilast 1; IFNβ (1); tofacitinib (1)

No association between the use of immunomodulatory treatment (CS and/or steroid sparing agent [SSA]) at the time of PD-(L)1 inhibitor initiation and response to immune CPI treatment (p = .66)

IFNβ. interferon beta; MTX, methotrexate; RA, rheaumatoid arthritis.

1. Gutzmer R et al. Eur J Cancer 2017;75:24–32. 2. Leonardi GC et al. J Clin Oncol 2018;36:19:1905–12.

Q3: Influence of the immunosuppressive treatment (used to treat baseline autoimmune disease) on the CPI response?



* 52 patients: anti-PD-1

20 under IS at start of the treatment (largest study available)

Treatment of AI disorder at PD1 start		
No immunosuppresion	32 (62%)	
Corticosteroids	9 (17%)	
Steroid-sparing agent	5 (10%)	Mesalamine 2, leflunomide, hydroxychloroquine, apremilast
Steroids and SSAs	5 (10%)	Sulfasalazine, leflunomide, hydroxychloroquine, methotrexate, ibuprofen
IVIG	1 (2%)	

* Similar response rate whether irAEs are present or not (35% vs 31%, n.s.)

* **Lower** response rate if IS at treatment initiation

3/20, 15% vs **14/32**, 44% **(p = 0.033)**, even if adjusted for prognostic factors

(AJCC stage, brain metastasis, ECOG PS, LDH; **p = 0.029**)

2 patients with CS alone responded; **none** with SSAs or combination CS+SSAs

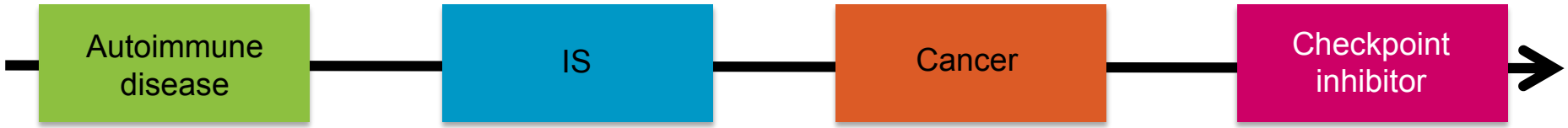
1 patient with IVIg responded

Concerns about IS baseline treatment !

ECOG PS, Eastern Cooperative Oncology Group Performance Status; LDH, lactate dehydrogenase.

Menzies AM et al. Annals of Oncology 2017;28:368–376.

Q3: Influence of the immunosuppressive treatment (used to treat baseline autoimmune disease) on the CPI response?

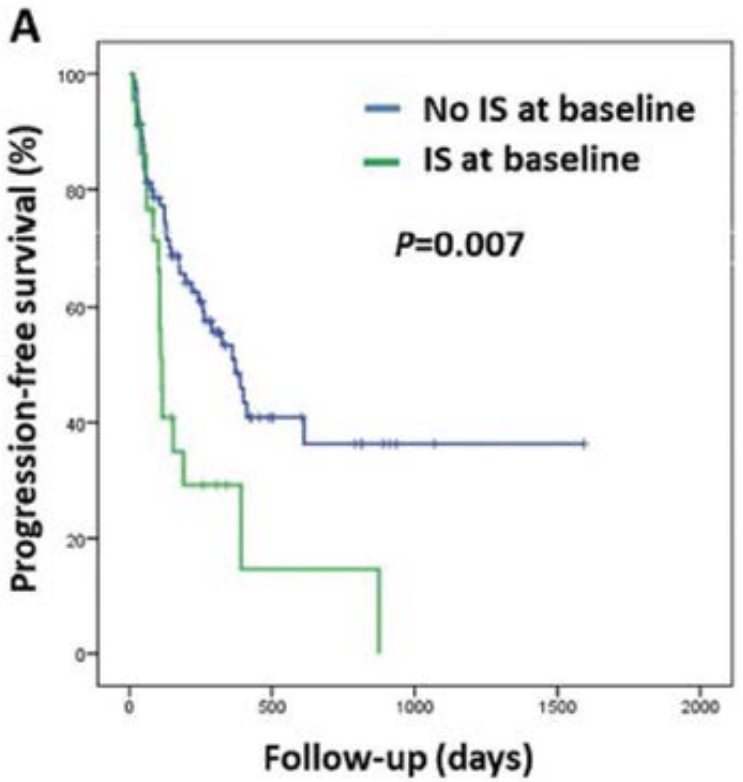


* 122 patients under CPI (retrospective study)
Abstract EULAR 2018

24 under IS at start of the treatment (largest abstract available)
10 GC
10 sDMARDS
1 rituximab

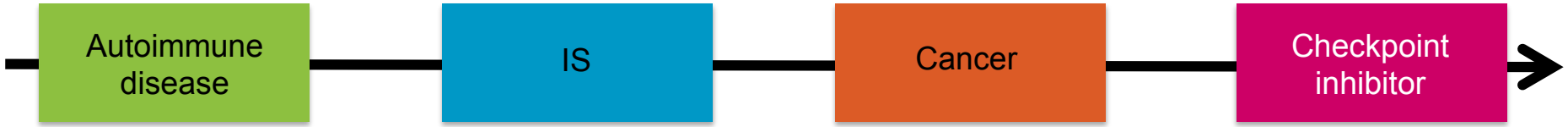
Higher rate of disease flare-ups (42%), with more than 1/3 that had to delay or stop the CPI

PFS and OS were shorter in patients with IS at baseline (**p = 0.007** and **p = 0.003**)



sDMARDs, synthetic disease-modifying antirheumatic drugs.

Intermediate conclusion



Not enough data to give strong recommendations about **baseline immunosuppressive treatment**

No strong evidence that active disease is at higher risk of recurrence than non-active disease

What about conventional sDMARDs?
Limited data, but we have concerns …

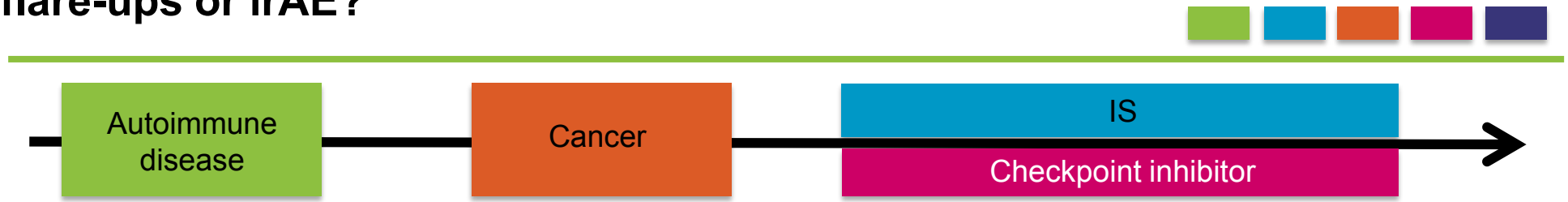
What about biological treatments?
No data, and we also have concerns …

TNFi: *in vitro* concerns, tumoral concerns
Abatacept (CTLA4Ig fusion protein): probably no
Rituximab (anti-CD20): probably no
Roactemra (anti-IL-6R): could be an option? But risk of GI perforation

TNFi, TNF inhibitor.

Q3: Influence of a prophylactic immunosuppressive treatment to avoid flare-ups or irAE?

Q3: Influence of a prophylactic immunosuppressive treatment to avoid flare-ups or irAE?



* 2 case reports for baseline active myositis

    * concerns about life-threatening disease flare-up risk
    * authors did not want to use TNFi or GC concomitant to CPI because previously ineffective or because concern for the CPI activity)

* **vedolizumab** (integrin inhibitor) administered 1 week before: no information on tumor response and unfortunately flare

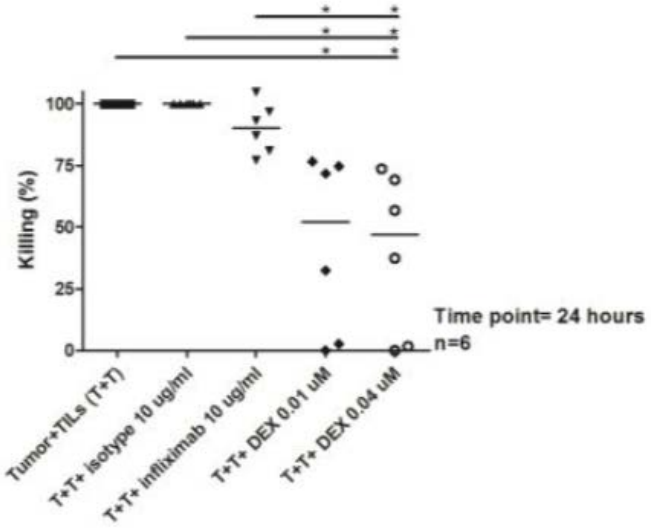
* **tocilizumab** (anti-IL6-R) administered concomitantly: tumor response, but colic abcess (flare-up or tocilizumab AEs?)

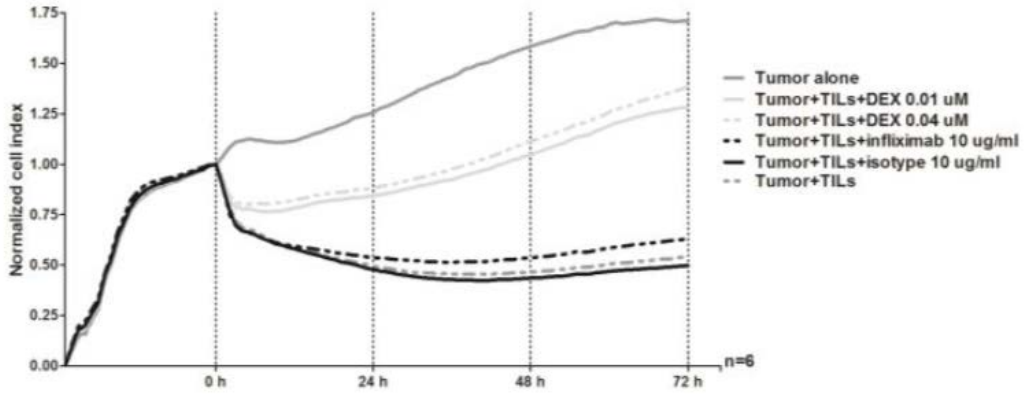
1. Uemura et al. Journal of Hematology & Oncology 2016;9:81. 2. Bergqvist V et all. Cancer Immunol Immunother 2017;66:581–592.

Q3: Influence of a prophylactic immunosuppressive treatment to avoid flare-ups or irAE?

* *In vitro* concerns about GC concomitant use

In vitro tumor killing activity of T lymphocytes with concomitant TNFi or GC
Index cell representing the number of tumor cells

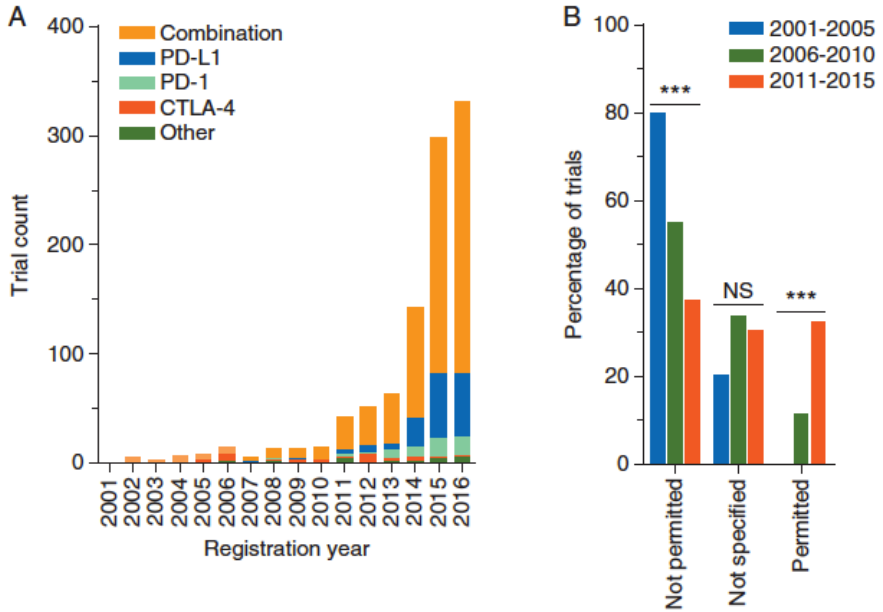




Q3: Influence of a prophylactic immunosuppressive treatment to avoid flare-ups or irAE?

* In *vivo* concerns about GC concomitant use?

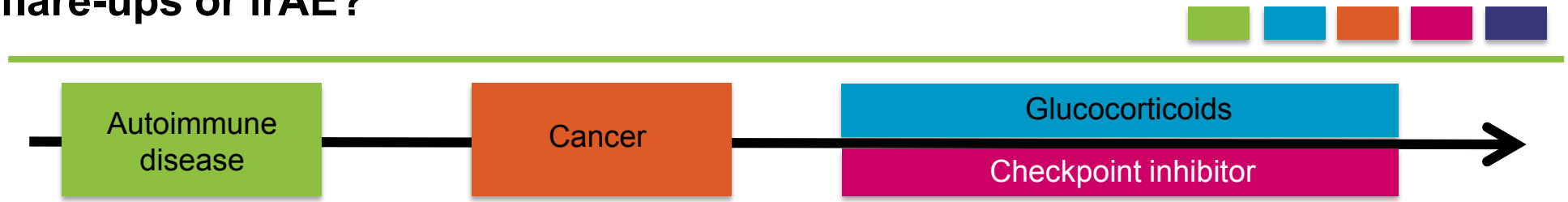
An emerging situation even in clinical trials



Connell CM et al. Annals of Oncology 2017;28:7:1678–79.

.

Q3: Influence of a prophylactic immunosuppressive treatment to avoid flare-ups or irAE?



* In *vivo* concerns about GC concomitant use?

Systematic review 2017: 10 research papers

* 8 without any influence, 2 with influence
* “the addition of CS to immunotherapy may not necessarily lead to poorer clinical outcomes”. Limited data!

Many limitations:

* GC were given
    * only for irAE n = 5. No outcome difference for these 5 studies
    * 1 study where GC were given for only non irAE reasons: outcome difference!

* Study inclusions finished in November 2016

* 8 studies about melanoma. No data about lung cancer (COPD patients, with frequent GC use)

COPD, chronic obstructive pulmonary disease.
Garant A et al. Critical Reviews in Oncology/Hematology 2017;120:86–92.

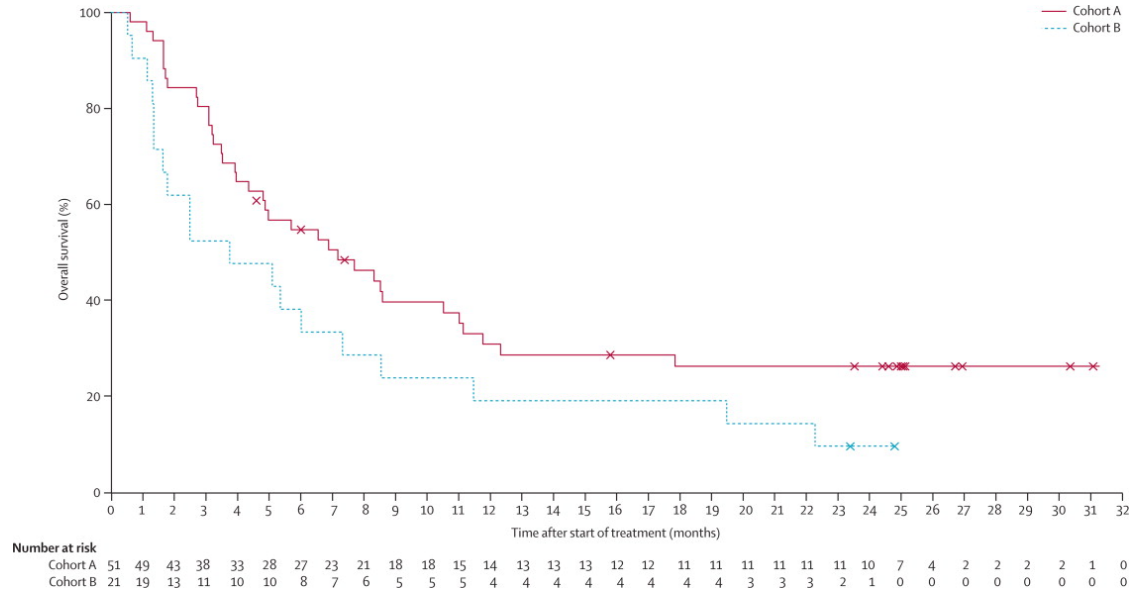
Q3: Influence of a prophylactic immunosuppressive treatment to avoid flare-ups or irAE?

* In *vivo* concerns about GC concomitant use ?

Ipilimumab in melanoma with brain metastasis

A : no neurological symptoms, no CS

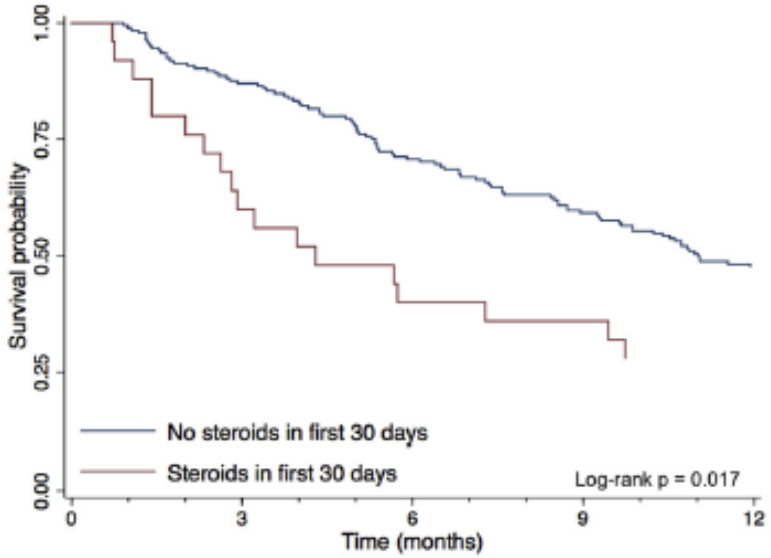
B : neurological symptoms, CS



Q3: Influence of a prophylactic immunosuppressive treatment to avoid flare-ups or irAE?

* In *vivo* concerns about GC concomitant use ?

210 patients with NSLC under nivolumab
66%: CS (COPD, brain metastasis)
Reasons:
27% brain metastasis
21% respiratory problems
18% constitutional symptoms
17% other indications
17% for irAE



Analysis of **early** exposure of CS (30 days) n = 25 (12%)

Median overall survival: 4.3 months (if early exposure) vs 11 months (if no CS)

Scott SC et al. Journal of Thoracic Oncology 2018;33:11:1771–75.

Q3: Influence of a prophylactic immunosuppressive treatment to avoid flare-ups or irAE?

* In *vivo* concerns about GC concomitant use?

Abstract ASCO June 2018

Patients with NSLC under anti PD-1 / PD-L1

2 centers (USA & France): n = 455 and n = 185

Inclusion: baseline oral or iv GC.

Very low dose GC (< 10 mg pred daily, n < 20): included in the non-GC group)

Response in GC/non-GC group: 6%/9% (n = 455); 8%/18% (n = 185)

Progression-free survival and overall were influenced by baseline GC ($p < 0.001$, regardless of age, sex, performance status, NSCLC histology and presence/absence of brain metastasis)

Authors: careful use of steroids at the time of initiating PD-1/PD-L1 blockade is recommended

Intermediate conclusion

Chronic and baseline use of GC should be considered independently from the use of GC in case of irAE!

In case of chronic and baseline GC treatment, when given independently from an irAE, *in vivo* concerns about the anti-tumoral efficacy

UZ LEUVEN

Managing patients with underlying autoimmune diseases:

Prof Eric Van Cutsem, MD, PhD
Digestive Oncology
Leuven, Belgium
Eric.VanCutsem@uzleuven.be

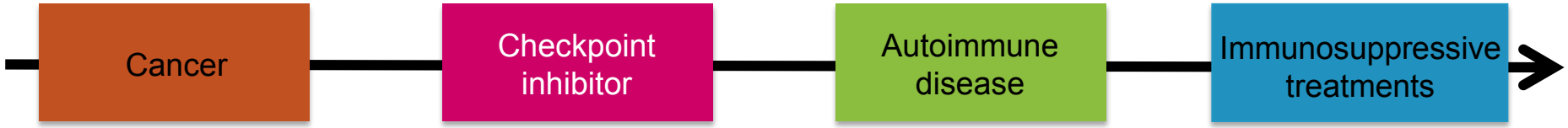
UZ Leuven | Herestraat 49 B - 3000 Leuven | www.uzleuven.be tel. +32 16 33 22 11

UNIVERSITY HOSPITALS LEUVEN

Disclosures

Receipt of grants/research supports:	Amgen, Bayer, BMS, Boehringer, Celgene, Ipsen, Lilly, Merck, Merck KgA, Novartis, Roche, Servier
Receipt of honoraria or consultation fees:	Bayer, BMS, Celgene, Lilly, Merck, Merck KgA, Novartis, Servier

Q4: Does treatment with steroid for underlying disease influence the efficacy of cancer treatment?



- Presently, a large number of clinical trials studying immune checkpoint inhibitors (ICI) exclude cancer patients who are on corticosteroids: this is based on the biological hypothesis that corticosteroids may antagonise the therapeutic effects of immunotherapy
- Few clinical data available:
  - Use of corticosteroids for ICI-related immune AEs: no evidence of impact on clinical outcome: several melanoma and lung studies
  - What about patients with underlying autoimmune disease, treated with corticosteroids?

ICI, immune checkpoint inhibitors.

Q4: Does treatment with steroid for underlying disease influence the efficacy of cancer treatment?

Author	Primary disease site	Presence of brain mets	Type of steroid	Steroid indication	Checkpoint name	Outcome reported	Median follow-up (mo)	# Patients	# Patients on steroids	Adult vs pediatric	Radiation given
Arriola et al. (2015)	Melanoma	No	Prednisolone	irAEs, pneumocystis jirovecii	Ipilimumab	OS, DCR	45	2	2	Adult	No
Barnett et al. (2017)	Duodenal adenocarcinoma	No	Prednisone	Organ transplant	Nivolumab	RR	18	1	1	Adult	No
Bernier et al. (2017)	Non-small cell lung	No	Prednisone, methylprednisone	irAEs	Nivolumab	RR	15	1	1	Adult	No
Foran et al. (2016)	Lymphoma	No	NOS	Chemotherapy prophylactic pre-medication	Nivolumab	DCR	11	1	1	Pediatric	No
Harmankaya et al. (2011)	Melanoma	No	Methylprednisone	irAEs	Ipilimumab	OS, DCR	24	1	1	Adult	No
Herz et al. (2016)	Melanoma	No	Dexamethasone, prednisone	Organ transplant	Nivolumab	DCR	NOS	4	2	Adult	Some
Kyi et al. (2014)	Melanoma	No	Prednisone	Known autoimmune disease	Ipilimumab	PFS	15	2	1	Adult	No
Lammert et al. (2013)	Melanoma, prostate	No	Multiple	irAEs	Ipilimumab	RECIST	12 to 16	7	7	Adult	No
Li et al. (2017)	Non-small cell lung	No	Prednisone	irAEs	Nivolumab	RR	14	1	1	Adult	Yes
Lipson et al. (2014)	Melanoma	No	Prednisone	irAEs, organ transplant	Ipilimumab	PFS	24	2	2	Adult	No
Lipson et al. (2016)	Skin SCC	No	Prednisone	irAEs, organ transplant	Pembrolizumab	RECIST	8	1	1	Adult	No
Luttmann et al. (2016)	Melanoma	Yes	Dexamethasone	Symptomatic metastases	Pembrolizumab	RECIST	12	1	1	Adult	No
Maul et al. (2016)	Melanoma	No	Prednisolone	Known autoimmune disease	Pembrolizumab	RECIST	11	1	1	Adult	No
Nguyen et al. (2016)	Melanoma	No	Prednisone, methylprednisone	irAEs	Pembrolizumab	RECIST	3 to 6	2	2	Adult	No
Parakh et al. (2016)	Melanoma	No	Prednisone	irAEs	Pembrolizumab	RECIST	12	1	1	Adult	No
Spain et al. (2016)	Melanoma	No	Prednisolone	irAEs	Nivolumab	RECIST	6 to 7	1	1	Adult	No
Villasboas et al.(2016)	Lymphoma	No	Prednisone	Stem cell transplant/GVHD	Pembrolizumab	RECIST	4 to 12	2	2	Adult	No

Adapted from Garant A et al. 2017

- Review: suggests that corticosteroids do not necessarily influence negatively the outcome on ICI

DCR, disease control rate; DOR, duration of response; NOS, not otherwise specified; ORR, overall response rate; OS, overall survival, PFS, progression-free survival; RECIST, response evaluation criteria in solid tumors; RR, response rate. Garant A et al. Critical Reviews in Oncology/Hematology 2017;120:86–92.

Q4: Does treatment with steroid for underlying disease influence the efficacy of cancer treatment?

- Retrospective study in 2 centers (MSKCC-NY, IGR-Villejuif) in 641 patients, of which 90 (14%) took > 10 mg prednisone

VOLUME 36 · NUMBER 28 · OCTOBER 1, 2018

JOURNAL OF CLINICAL ONCOLOGY

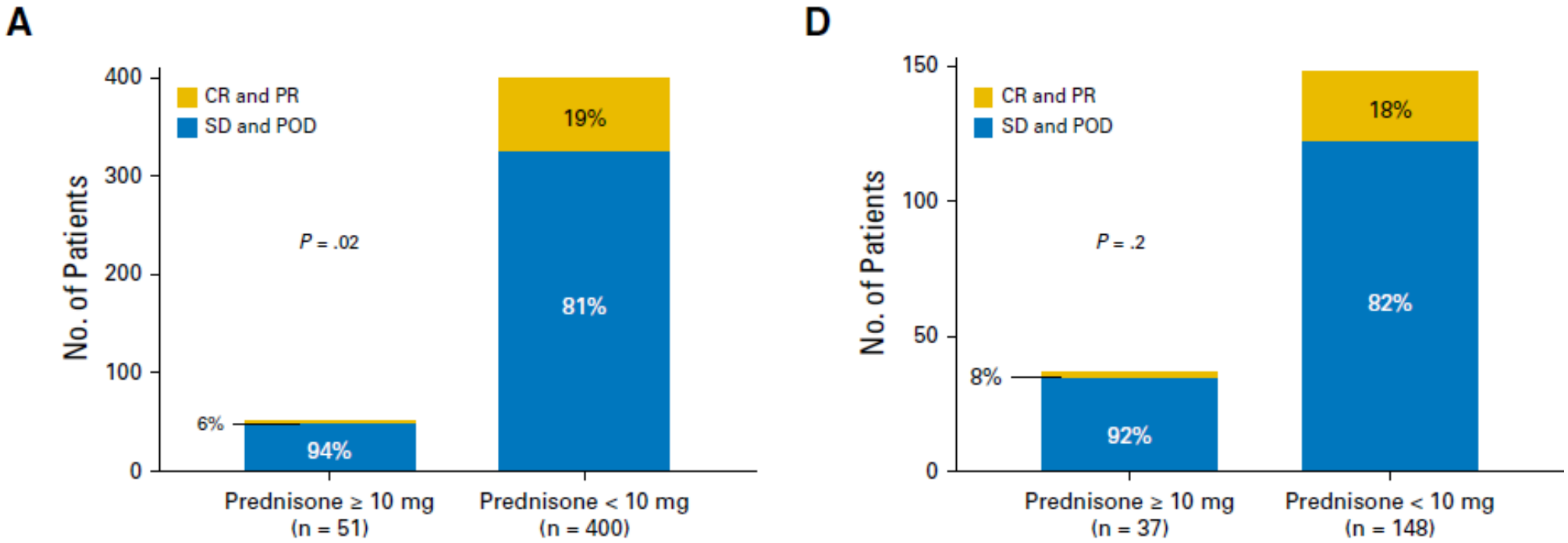
ORIGINAL REPORT

Impact of Baseline Steroids on Efficacy of Programmed Cell Death-1 and Programmed Death-Ligand 1 Blockade in Patients With Non–Small-Cell Lung Cancer

Kathryn C. Arbour, Laura Mezquita, Niamh Long, Hira Rizvi, Edouard Auclin, Andy Ni, Gala Martínez-Bernal, Roberto Ferrara, W. Victoria Lai, Lizza E.L. Hendriks, Joshua K. Sabari, Caroline Caramella, Andrew J. Plodkowski, Darragh Halpenny, Jamie E. Chaft, David Planchard, Gregory J. Riely, Benjamin Besse, and Matthew D. Hellmann

Arbour et al. J Clin Oncol 2018;36:2872–78.

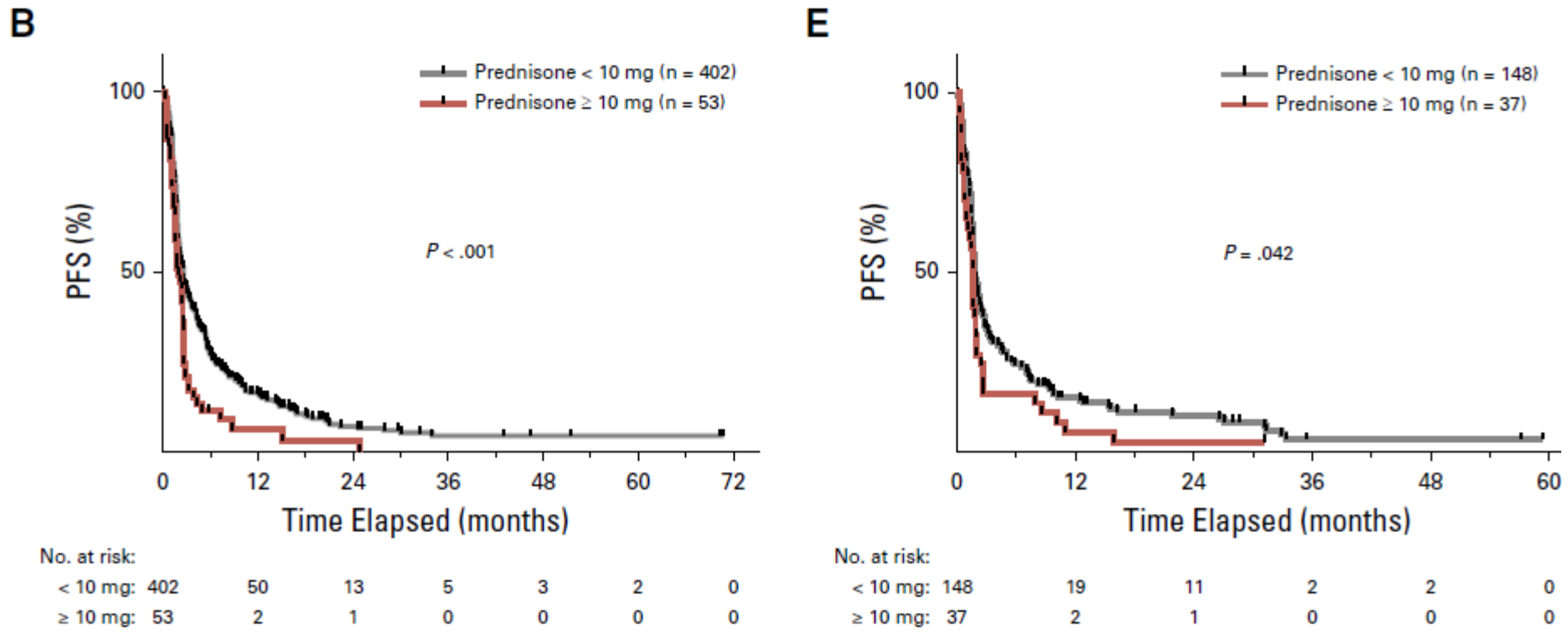
Q4: Does treatment with steroid for underlying disease influence the efficacy of cancer treatment



► Fig 1. Response rates (A and D), PFS (B and E), and OS (C and E) of patients treated with programmed death-ligand 1 blockade on the basis of reported corticosteroid usage at Memorial Sloan Kettering Cancer Center (MSKCC; A-C) and Gustave Roussy Cancer Center (GRCC; D-F). Four hundred fiftyone of 455 patients were evaluable for response in the MSKCC cohort (A) and 185 of 185 patients were evaluable for response in the GRCC cohort (D)

CR, complete response; POD, progression of disease; PR, partial response; SD, stable disease.
Arbour et al. J Clin Oncol 2018;36:2872–78.

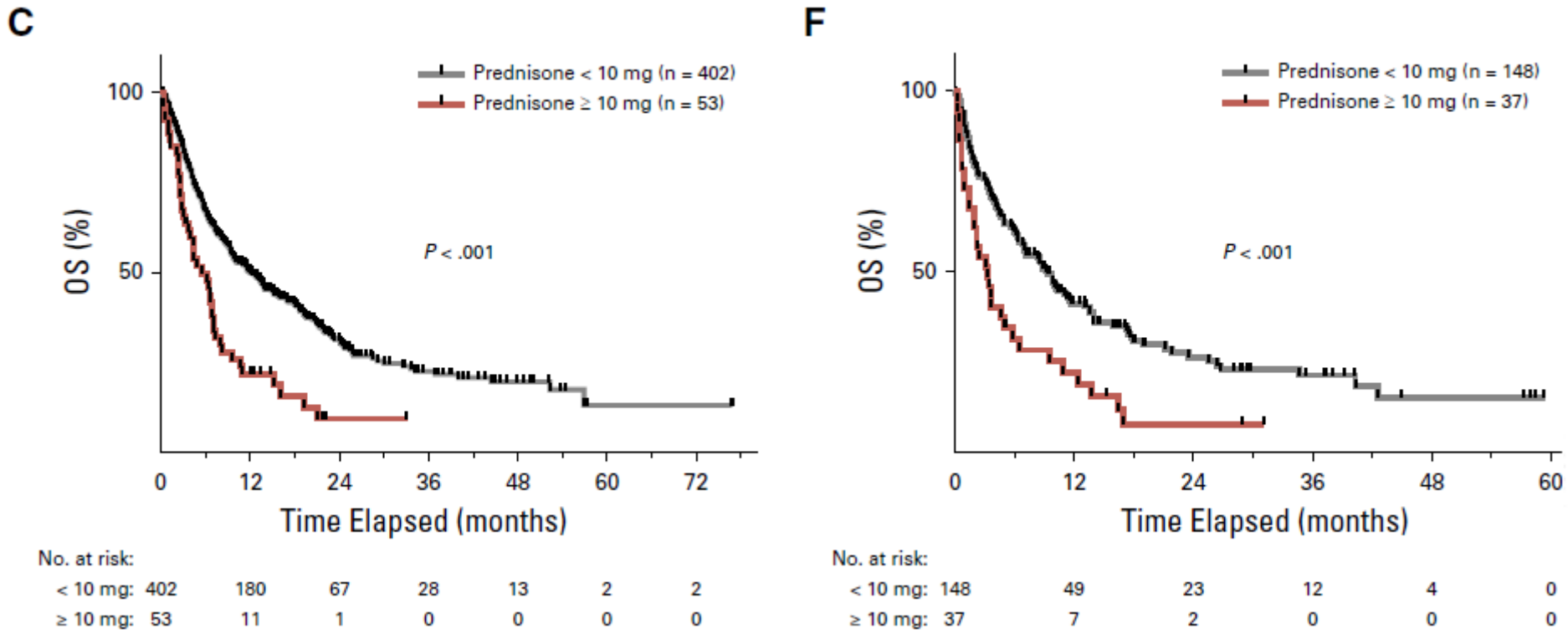
Q4: Does treatment with steroid for underlying disease influence the efficacy of cancer treatment?



- Fig 1. Response rates (A and D), PFS (B and E), and OS (C and E) of patients treated with programmed death-ligand 1 blockade on the basis of reported corticosteroid usage at Memorial Sloan Kettering Cancer Center (MSKCC; A-C) and Gustave Roussy Cancer Center (GRCC; D-F). Four hundred fiftyone of 455 patients were evaluable for response in the MSKCC cohort (A) and 185 of 185 patients were evaluable for response in the GRCC cohort (D)

Arbour et al. J Clin Oncol 2018;36:2872–78.

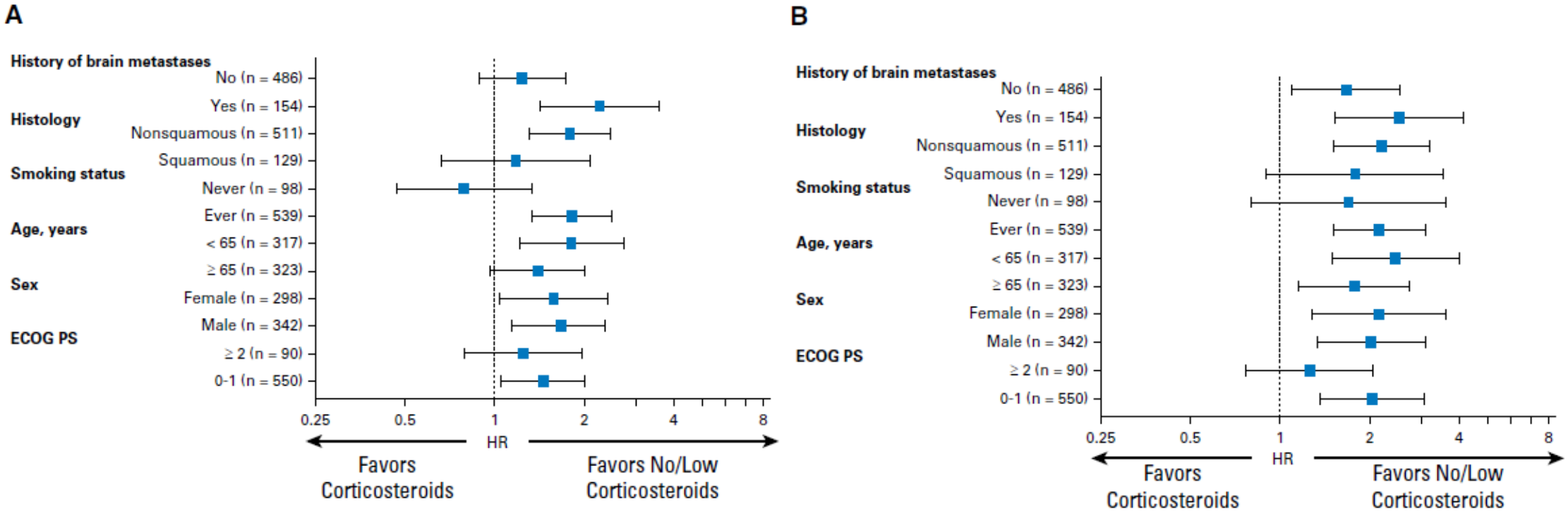
Q4: Does treatment with steroid for underlying disease influence the efficacy of cancer treatment?



- Fig 1. Response rates (A and D), PFS (B and E), and OS (C and E) of patients treated with programmed death-ligand 1 blockade on the basis of reported corticosteroid usage at Memorial Sloan Kettering Cancer Center (MSKCC; A-C) and Gustave Roussy Cancer Center (GRCC; D-F). Four hundred fiftyone of 455 patients were evaluable for response in the MSKCC cohort (A) and 185 of 185 patients were evaluable for response in the GRCC cohort (D)

Arbour et al. J Clin Oncol 2018;36:2872–78.

Q4: Does treatment with steroid for underlying disease influence the efficacy of cancer treatment?



- Fig 2. Forest plot of subgroup analyses of independent prognostic factors for (A) PFS and (B) OS in the pooled cohort (Memorial Sloan Kettering Cancer Center and Gustave Roussy Cancer Center combined)

ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; PS, performance status.
Arbour et al. J Clin Oncol 2018;36:2872–78.

Q4: Does treatment with steroid for underlying disease influence the efficacy of cancer treatment?

- Conclusion
  - Baseline corticosteroid use of ≥ 10 mg of prednisone equivalent was associated with poorer outcome in patients with non-small cell lung cancer who were treated with PD-(L)1 blockade
  - Prudent use of corticosteroids at the time of initiating PD-(L)1 blockade is recommended

Arbour et al. J Clin Oncol 2018;36:2872–78.


ImmunoScience Academy
Partnering for Education & Optimizing Treatment in ImmunoScience

Thank you

Disclaimer

While Bristol-Myers Squibb uses reasonable efforts to include accurate and up-to-date information in this material, Bristol-Myers Squibb makes no warranties or representations as to its accuracy. Bristol-Myers Squibb assumes no liability or responsibility for any errors or omissions in the content of the material. Neither Bristol-Myers Squibb nor any other party involved in creating, producing or delivering the material is liable for any direct, incidental, consequential, indirect or punitive damages arising out of your access to, or use of, the material.

You should assume that everything you see or read on this presentation is copyrighted, unless otherwise noted, and may not be used without mentioning the source. Bristol-Myers Squibb neither warrants nor represents that your use of materials displayed on the Site will not infringe rights of third parties not owned by or affiliated with Bristol-Myers Squibb.

Nothing on these presentations should be construed as the giving of advice or the making of a recommendation and it should not be relied on as the basis for any decision or action. BMS, nor other parties involved, accepts no liability for the accuracy or completeness or use of, nor any liability to update, the information contained on this Presentation. These materials are provided "AS IS" WITHOUT WARRANTY OF ANY KIND, EITHER EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, THE IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT.