A patient's journey through the immuno-oncology treatment landscape in melanoma

Disclaimer

- *Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions.*
- *The presenting faculty have been advised by touchIME to ensure that they disclose any such references made to unlabelled or unapproved use.*
- *No endorsement by touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in touchIME activities.*
- *touchIME accepts no responsibility for errors or omissions.*

touch IMMUNOLOGY

Impact of PD-1 inhibitors on patient journey and treatment experience: learnings from long-term and real-world data

Prof. Caroline Robert

Medical Oncologist and Head of Dermatology Unit
Goustave Roussy, Paris, France

touch IMMUNOLOGY

PD-1 blockade: Long-term (five-year) efficacy insights

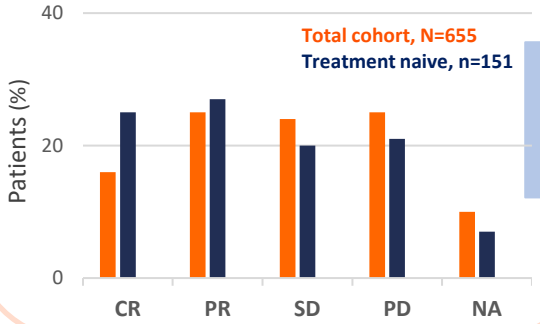
KEYNOTE-001[1]

Advanced/metastatic melanoma
(previously treated or treatment naive)

PEMBRO 2 mg/kg ***or*** 10 mg/kg Q3W ***or*** 10 mg/kg Q2W

	Total cohort N=655	Treatment naive n=151
mPFS, months	8.3	38.6
mOS, months	23.8	16.9

Best overall response



Confirmed the durable and robust tumour activity and safety of pembrolizumab

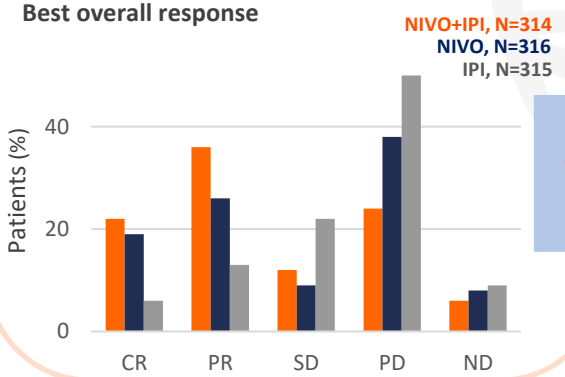
CheckMate-067[2]

Treatment-naive advanced melanoma

NIVO 1 mg/kg **+ IPI** 3 mg/kg Q3W x 4 doses followed by NIVO 3 mg/kg Q2W
NIVO 3 mg/kg Q2W **+ IPI-matched placebo**
IPI 3 mg/kg Q3W **+ NIVO-matched placebo**

	NIVO+IPI N=314	NIVO N=316	IPI N=315
mPFS, months	11.5	6.9	2.9
mOS, months	>60.0*	36.9	19.9

Best overall response



NIVO+IPI or NIVO alone was associated with sustained long-term OS at 5 years

*median not reached. CI, confidence interval; CR, complete response; IPI, ipilimumab; mOS, median overall survival; NA, no assessment; ND, not able to determine; NIVO, nivolumab; NR, not reached; PEMBRO, pembrolizumab; mPFS, median progression-free survival; PD, progressive disease; PD-1, programmed cell death protein-1; PR, partial response; Q2W, every 2 weeks; Q3W, every 3 weeks; SD, stable disease.

1. Hamid O, et al. *Ann Oncol.* 2019;30:582–8; 2. Larkin J, et al. *New Engl J Med*. 2019;381:1535–46.

touch IMMUNOLOGY

PD-1 blockade: Long-term (five-year) safety insights

KEYNOTE-001[1]

Advanced melanoma
(previously treated or treatment-naive)

86% Experienced TRAEs → **7.8%** Study discontinuation

17% Grade 3/4 TRAEs

Long-term tolerability of pembrolizumab was confirmed in this five-year analysis

CheckMate-067[2]

Treatment-naive advanced melanoma

	NIVO+IPI N=313	NIVO N=313	IPI N=315
Grade 3/4 TRAEs	59%	23%	28%
Discontinuation	42%	13%	15%

Safety results from this five-year analysis were similar to previously reported results for regimens containing nivolumab

Biomarker needed to predict response in order to spare patients toxicity risk

IPI, ipilimumab; NIVO, nivolumab; PD-1, programmed cell death protein-1; PEMBRO, pembrolizumab; Q2W, every 2 weeks; Q3W, every 3 weeks; TRAEs, treatment-related adverse events.

1. Hamid O, et al. *Ann Oncol.* 2019; 2. Larkin J, et al. *New Engl J Med*. 2019;381:1535–46.

touch IMMUNOLOGY

Adjuvant PD-1 blockade: Long-term RFS benefit

KEYNOTE-054[1]

Completely resected stage III melanoma

PEMBRO 200 mg Q3W (n=514)
Placebo Q3W (n=505)
18 doses over ~1 year

Median follow-up: 36.6 months

3-year RFS, rate, %
ITT overall population

PEMBRO	Placebo	HR
63.7%	44.1%	0.56 (95% CI 0.47–0.68)

Adjuvant PD-1 blockade in resected high-risk stage III melanoma achieved and sustained clinically meaningful improvement in long-term RFS

CheckMate-238[2]

Resected stage IIIB–C or IV melanoma

NIVO 3 mg/kg Q2W + matched placebo (n=453)
IPI 10 mg/kg Q3W + matched placebo (n=453)
For up to 1 year

Median follow-up: 51.1 months

4-year RFS, rate %
Overall population

NIVO	IPI	HR
51.7%	41.2%	0.76 (95% CI 0.60–0.86)

Adjuvant PD-1 blockade demonstrated sustained RFS benefit compared with adjuvant CTLA-4 blockade in resected stage IIIB–C or IV melanoma

CI, confidence interval; CTLA-4, cytotoxic T lymphocyte-associated antigen-4; HR, hazard ratio; IPI, ipilimumab; ITT, intention to treat; NIVO, nivolumab; PD-1, programmed cell death protein-1; PEMBRO, pembrolizumab; PFS, progression-free survival; RFS, recurrence-free survival.

1. Eggermont AMM, et al. *J Clin Oncol.* 2020;38:doi: 10.1200/JCO.20.02110; 2. Ascierto PA, et al. *Lancet Oncol.* 2020; doi: 10.1016/S1470-2045(20)30494-0.

touch IMMUNOLOGY

Adjuvant TT in melanoma: Learnings from COMBI-AD

Patients with resected stage III melanoma with *BRAF* V600E and V600K mutations

DAB + TRA
N=438

PLACEBO
N=432

Patients alive without relapse at 5 years: overall cohort

DAB + TRA **52%**

PLACEBO **36%**

HR 0.51
relapse or death 95% CI 0.42–0.61

Patients alive without relapse at 5 years: by disease stage

IIIA	65% / 58%	**HR 0.61** relapse or death	95% CI 0.35–1.07
IIIB	55% / 34%	**HR 0.50** relapse or death	95% CI 0.37–0.67
IIIC	45% / 29%	**HR 0.48** relapse or death	95%CI 0.36–0.64

BID, twice daily; *BRAF*, B-Raf proto-oncogene; CI, confidence interval; CR, complete response; DAB, dabrafenib; HR, hazard ratio; ICI, immune checkpoint inhibitor; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; QD, once daily; RFS, relapse-free survival; SD, stable disease; TRA, trametinib; TT, targeted therapy.

Dummer R, et al. *New Engl J Med.* 2020;383:1139–48.

touch IMMUNOLOGY

Long-term remission: Achievable post-discontinuation?

Finding the balance to maximize clinical benefit and minimize serious toxicity risk

~20%

treated with PD-1 blockade ± anti-CTLA-4 achieve CR[1]

after SIX months

can consider discontinuation in these patients

KEYNOTE-001 and KEYNOTE-006

Optimal duration of PD-1 blockade after CR

On achieving CR

91%

maintained CR after a medium of ~24 months after discontinuing PD-1 blockade[2]

~86%

who stopped PD-1 blockade early after at least 6 months remained progression free at 24 months[3]

CR, complete response; CTLA-4, anti-cytotoxic T lymphocyte-associated antigen-4; PD-1, programmed cell death protein-1;.

1. Robert C, et al. *Nat Commun.* 2020;11:3801; 2. Robert C, et al. *J Clin Oncol.* 2018;36:1668–74; 3. Robert C, et al. *Lancet Oncol.* 2019;20:1239–51.

touch IMMUNOLOGY

Transparent communication underpins melanoma care

Building trusted relationships facilitates patient–physician conversations

Transparency

Keep the patient informed to facilitate shared decision-making and build trust

Regular follow-up

Build relationship and a rapport with patients and their caregivers at follow-ups

Patient-centred care

Know the concerns and individual needs of each patient for consideration in decisions surrounding treatment and care

Shared decision-making

Empower patients to engage with their care and treatment decisions as an equal

Effectively managing conversations with patients and their caregivers in the event of relapse requires trust and understanding, founded in an established and ongoing ‘partnership’ between physicians and patients

Kaba R and Sooriakumaran P. *Int J Surgery.* 2007;5:57–65.