Melanoma update

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Conflicts

- **Amgen**
- **Astra-Zeneca**
- **BMS**
- **Incyte**
- **Janssen (J&J)**
- **Merck**
- **Novartis**
- **Pfizer**
- **Regeneron**
- **Sanofi**

NB possible mentions of *Off-label* drug use

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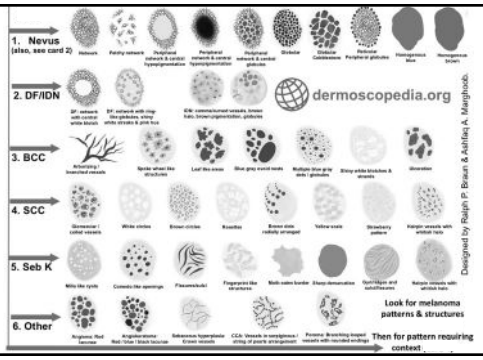
Outline

- **Melanoma Staging**
  - **Diagnosis: dermoscopy and biopsy**
  - **AJCC classification**
  - **Pathological evaluation**
  - **Nodal status: clinical or SLNB**
- **Types of melanoma treatments:**
  - **Metastatic**
  - **Adjuvant**
  - **Neoadjuvant**
- **Conclusion**

3



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Essential: a good biopsy

5

FROM THE ACADEMY

Guidelines of care for the management of primary cutaneous melanoma

Work Group: Susan M. Swetter, MD (Chair),[a,b] Hensin Tsao, MD, PhD (Co-Chair),[c,d] Christopher K. Bichakjian, MD,[e,f] Clara Curiel-Lewandrowski, MD,[g,h] David E. Elder, MBChB,[i,j] Jeffrey E. Gershenwald, MD,[k,l] Valerie Guild, MS, MBA,[m] Jane M. Grant-Kels, MD,[n,o,p] Allan C. Halpern, MD,[q] Timothy M. Johnson, MD,[r,s] Arthur J. Sober, MD,[t] John A. Thompson, MD,[u,v] Oliver J. Wisco, DO,[f] Samantha Wyatt, MD,[w] Shasa Hu, MD,[x] and Toyin Lamina, PhD[w]
Stanford and Palo Alto, California; Boston, Massachusetts; Ann Arbor, Michigan; Tucson, Arizona; Philadelphia, Pennsylvania; Houston and Plano, Texas; Farmington, Connecticut; New York, New York; Seattle, Washington; Portland, Oregon; Decatur, Alabama; Miami, Florida; and Rosemont, Illinois

The incidence of primary cutaneous melanoma continues to increase each year. Melanoma accounts for the majority of skin cancer–related deaths, but treatment is usually curative following early detection of disease. In this American Academy of Dermatology clinical practice guideline, updated treatment

J Am Acad Dermatol
Volume 80, Number 1

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January 2019

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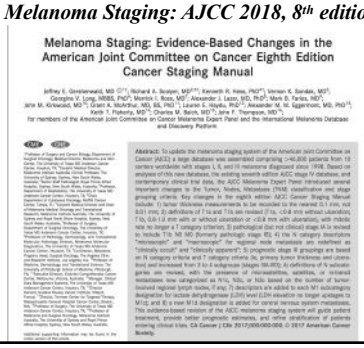
Melanoma Staging: AJCC 2018, 8th edition



Melanoma Staging: Evidence-Based Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual

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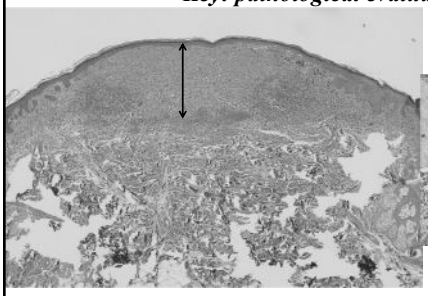
Key: pathological evaluation



Breslow thickness

Ulceration

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Initial work-up: stage IIB, IIC, III

(Breslow > 2 mm and ulceration or > 4 mm or any nodal disease)

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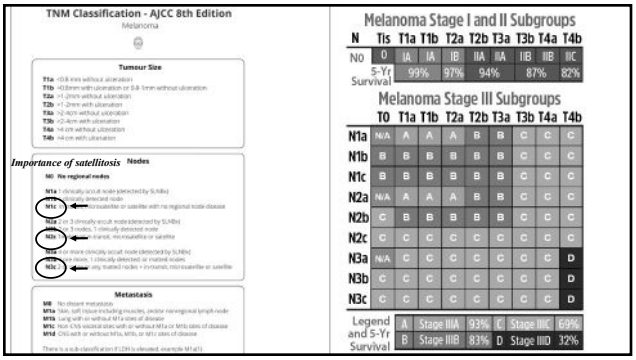

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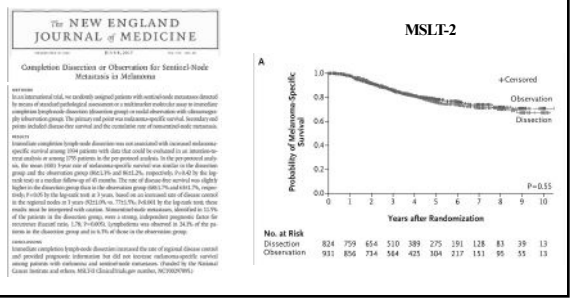
No more Complete lymph node dissection if SLNB+



The NEW ENGLAND JOURNAL of MEDICINE

Completion Dissection or Observation for Sentinel-Node Metastasis in Melanoma

MSLT-2

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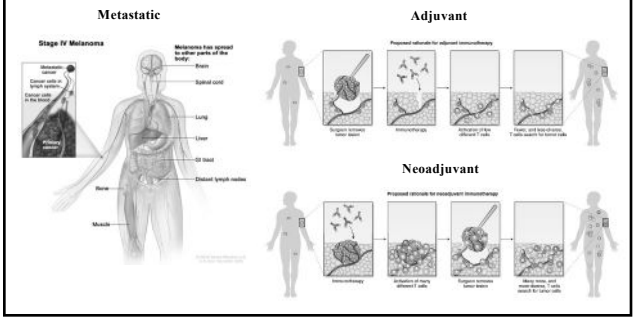
Types of Melanoma therapies



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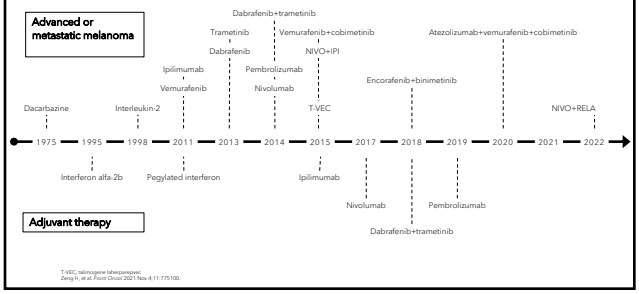
Timeline of Approved Melanoma Therapies



T-VEC, talimogene laherparepvec
Zeng H, et al. Front Oncol 2021 Nov 4;11:775100.

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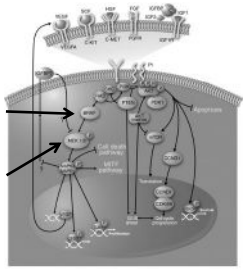
Targeted therapies– MAPK pathway



Anti-BRAF:
Dabrafenib
or Vemurafenib
or Encorafenib

Anti-MEK:
Trametinib
or Cobimetinib
or Binimetinib

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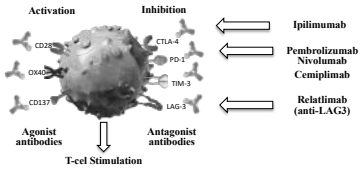
Checkpoint controls of T lymphocytes



Dianis Mellman et al. Nature 2011; 480(7378): 480-9. Pardoll DM. Nat Rev Cancer 2012; 12(4): 252-64.

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Pembrolizumab: 10-year update

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Pembrolizumab vs Ipilimumab for Advanced Melanoma: 10-Year Follow-Up of the Phase 3 KEYNOTE-006 Study

Caroline Robert[1]; Matteo S. Carlino[2-4]; Catriona McNeil[5]; Antoni Ribas[6]; Jacob Schachter[7]; Marta Nyakas[8]; Damien Kee[9]; Teresa M. Petrella[10]; Arnold Blaustein[11]; Michal Lotem[12]; Ana M. Arance[13]; Adil I. Daud[14]; Omid Hamid[15]; James Larkin[16]; Lili Yao[17]; Rohini Singh[17]; Rohit Lal[17]; Georgina V. Long[2,3,18,19]

[1]Gustave Roussy and Paris-Saclay University, Villejuif, France; [2]Melanoma Institute Australia, The University of Sydney, Sydney, NSW, Australia; [3]Faculty of Medicine & Health, The University of Sydney, Sydney, NSW, Australia; [4]Westmead and Blacktown Hospitals, Sydney, NSW, Australia; [5]Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [6]Jonsson Comprehensive Cancer Center at University of California Los Angeles (UCLA), Los Angeles, CA, USA; [7]Sheba Medical Center-Tel HaShomer, Ramat Gan, Israel; [8]Oslo University Hospital, Oslo, Norway; [9]Austin Health, Heidelberg, VIC, Australia; [10]Sunnybrook Health Sciences Centre, Toronto, ON, Canada; [11]Mount Sinai Medical Center Comprehensive Cancer Center, Miami Beach, FL, USA; [12]Sharett Institute of Oncology, Hadassah University Hospital Ein Kerem, Jerusalem, Israel; [13]Hospital Clinic Barcelona and IDIBAPS, Barcelona, Spain; [14]University of California San Francisco, San Francisco, CA, USA; [15]The Angeles Clinic and Research Institute, a Cedars-Sinai Affiliate, Los Angeles, CA, USA; [16]The Royal Marsden NHS Foundation Trust, London, United Kingdom; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Charles Perkins Centre, The University of Sydney, Sydney, NSW, Australia; [19]Royal North Shore and Mater Hospitals, Sydney, NSW, Australia

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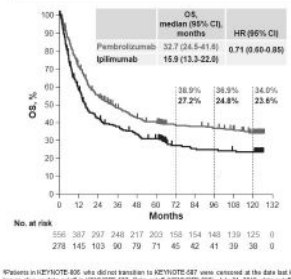
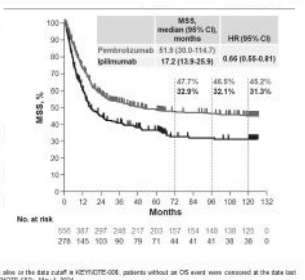
Overall Survival[a]



Melanoma-Specific Survival



[a]Patients in KEYNOTE-006 who did not transition to KEYNOTE-587 were censored at the date last known alive or the data cutoff in KEYNOTE-006; patients without an OS event were censored at the date last known alive or data cutoff in KEYNOTE-587. Data cutoff (KEYNOTE-006): July 31, 2019; data cutoff (KEYNOTE-587): May 1, 2024.

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Ipi-Nivo: 10-year update

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BARCELONA 2024 ESMO congress

10-Year survival outcomes from the phase 3 CheckMate 067 trial of nivolumab plus ipilimumab in advanced melanoma

James Larkin,[1] Vanna Chiarion-Sileni,[2] Caroline Gaudy-Marqueste,[3] Piotr Rutkowski,[4] Teresa Medina,[5] Christopher D. Lao,[6] C. Lance Cowey,[7] Dirk Schadendorf,[8] John Wagstaff,[9] Reinhard Dummer,[10] Paola Queirolo,[11] John Walker,[12] Marcus O. Butler,[13] Andrew G. Hill,[14] Iván Márquez Rodas,[15] John B.A.G. Haanen,[16] Ayman Nassar,[17] Margarita Askelson,[17] F. Stephen Hodi,[18*] Jedd D. Wolchok[19*]

[1]The Royal Marsden Hospital, London, United Kingdom; [2]Veneto Institute of Oncology IOV-IRCCS, Padua, Italy; [3]Timone Hospital, Aix-Marseille University, Marseille, France; [4]Maria Sklodowska Curie National Institute of Oncology, Warsaw, Poland; [5]University of Colorado Cancer Center, Aurora, CO, USA; [6]University of Michigan, Rogel Cancer Center, Ann Arbor, MI, USA; [7]Texas Oncology-Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA; [8]University Hospital Essen and the German Cancer Consortium, Essen, Germany; [9]The College of Medicine, Swansea University, Swansea, United Kingdom; [10]University of Zurich, Zurich, Switzerland; [11]European Institute of Oncology IRCCS, Milan, Italy; [12]University of Alberta, Cross Cancer Institute, Edmonton, AB, Canada; [13]UHN Princess Margaret Cancer Centre, Toronto, ON, Canada; [14]Tasman Oncology Research, Southport, QLD, Australia; [15]Hospital General Universitario Gregorio, Marañón, Madrid, Spain; [16]Netherlands Cancer Institute, Amsterdam, Netherlands; [17]Bristol Myers Squibb, Princeton, NJ, USA; [18]Dana-Farber Cancer Institute, Boston, MA, USA; [19]Sandra and Edward Meyer Cancer Center, Weill Cornell Medicine, New York, NY, USA
[Christopher D. Lao's current affiliation is Bristol Myers Squibb, Princeton, NJ, USA.]
*Co-senior authors.

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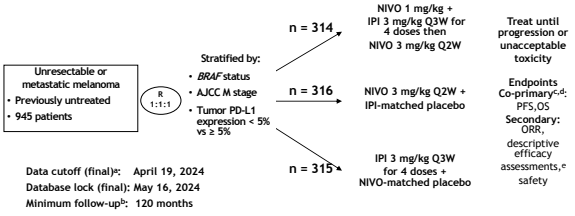
CheckMate 067: study design and follow-up length



Data cutoff (final)[a]: April 19, 2024
Database lock (final): May 16, 2024
Minimum follow-up[b]: 120 months

[a]No patient was being treated on study at the time of the final DBL. [b]From the date the last patient was randomized. [c]The study was not powered for a comparison between NIVO + IPI and NIVO. [d]NIVO + IPI or NIVO alone vs IPI. [e]NIVO + IPI vs NIVO alone.

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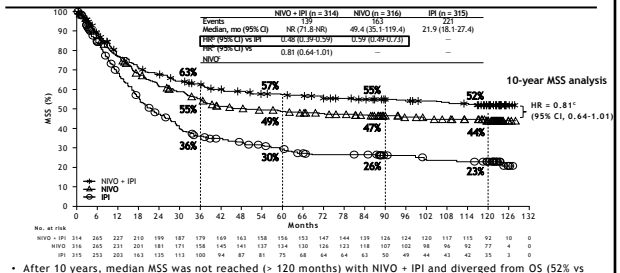
Melanoma-specific survival (MSS)[a]



- After 10 years, median MSS was not reached (> 120 months) with NIVO + IPI and diverged from OS (52% vs 43%)
  - Results were consistent by BRAF mutation and PD-L1 expression status (Supplemental Figures S1 and S2)

[a]In this post hoc descriptive analysis, an event was defined as death due to melanoma or euthanasia due to disease progression; any other death was censored. [b]Unstratified. [c]Descriptive comparison.

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Safety Summary

Patients reporting event	NIVO+IPI (n = 313) Any grade	NIVO+IPI (n = 313) Grade 3/4	NIVO (n = 313) Any grade	NIVO (n = 313) Grade 3/4	IPI (n = 311) Any grade	IPI (n = 311) Grade 3/4
Treatment-related AE, %	96	59	87	23	86	28
Treatment-related AE leading to discontinuation, %	42	31	13	8	15	14
Treatment-related death, n (%)	2 (1)		1 (< 1)		1 (< 1)	

- Survival outcomes were not impacted by discontinuing NIVO+IPI early due to a TRAE[b]
  - Patients who discontinued NIVO+IPI during induction due to a TRAE had 5-year PFS (35%) and OS rates (51%) similar to patients in the overall population (36% and 52%, respectively)

[a]Previously reported treatment-related deaths were cardiomyopathy and liver necrosis for NIVO+IPI (n = 1 each; both occurred > 100 days after last treatment), neutropenia for NIVO (n = 1), and colonic perforation for IPI (n = 1). [b]Post-hoc analysis. TRAE, treatment-related adverse event.

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Immunotherapy: side effects

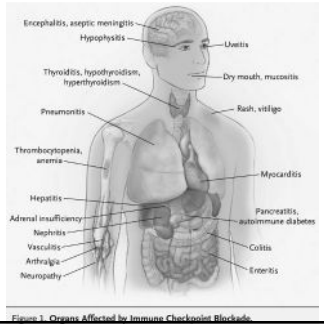

Figure 1. Organs Affected by Immune Checkpoint Blockade.

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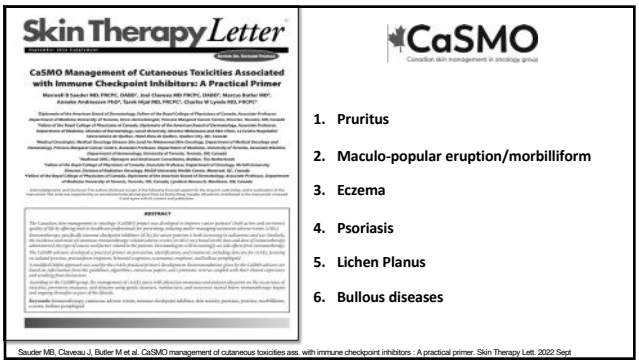

Sauder MB, Claveau J, Butler M et al. CaSMO management of cutaneous toxicities ass. with immune checkpoint inhibitors : A practical primer. Skin Therapy Lett. 2022 Sept

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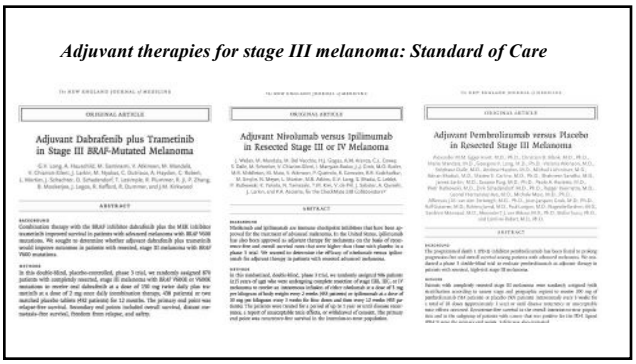

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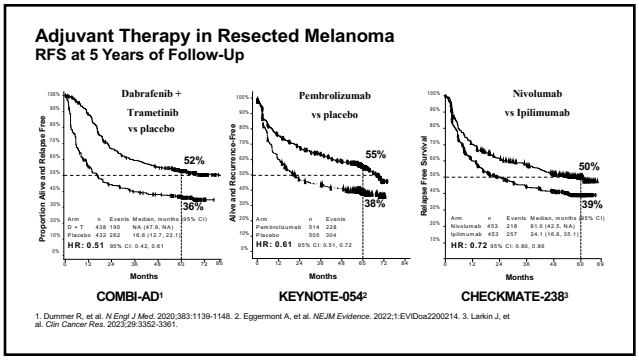

1. Dummer R, et al. *N Engl J Med.* 2020;383:1139-1148. 2. Eggermont A, et al. *NEJM Evidence.* 2022;1:EVIDoa2200214. 3. Larkin J, et al. *Clin Cancer Res.* 2023;29:3352-3361.

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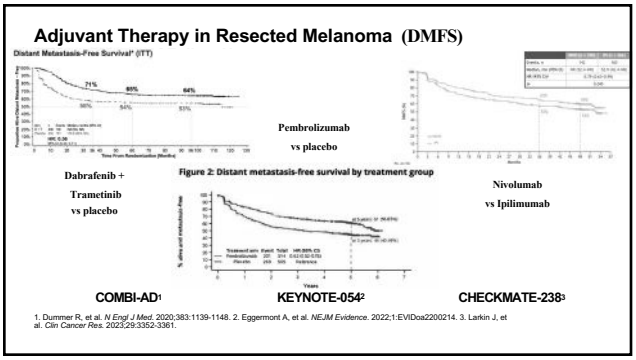

1. Dummer R, et al. *N Engl J Med.* 2020;383:1139-1148. 2. Eggermont A, et al. *NEJM Evidence.* 2022;1:EVIDoa2200214. 3. Larkin J, et al. *Clin Cancer Res.* 2023;29:3352-3361.

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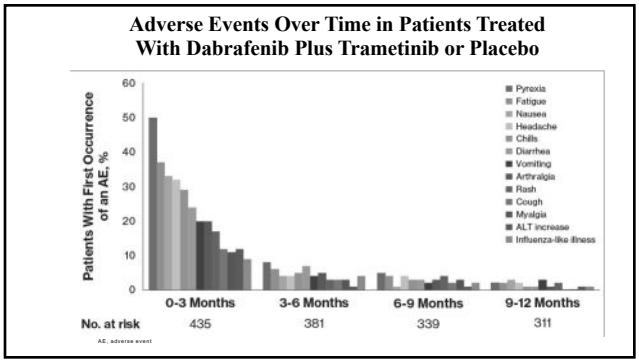

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Most recent: Adjuvant for Stage II disease

30

1615P

Pembrolizumab Versus Placebo as Adjuvant Therapy for Resected Stage IIB or IIC Melanoma: 5-Year Follow-Up of the Phase 3 KEYNOTE-716 Study

J. J. Luke[1]; G. V. Long[2]; M. A. Khattak[3]; P. Rutkowski[4]; M. Del Vecchio[5]; F. Spagnolo[6]; J. Mackiewicz[7]; L. de la Cruz Merino[8]; J. Pigozzo[9]; J. M. Kirkwood[10]; C. Robert[11]; M. S. Carlino[12]; D. Schadendorf[13]; F. De Galitiis[14]; A. Odeleye-Ajakaye[15]; T. Hoki[15]; M. Fukunaga-Kalabis[15]; A. M. M. Eggermont[15,16]; P. A. Ascierto[17]

Figure 1. KEYNOTE-716 study design

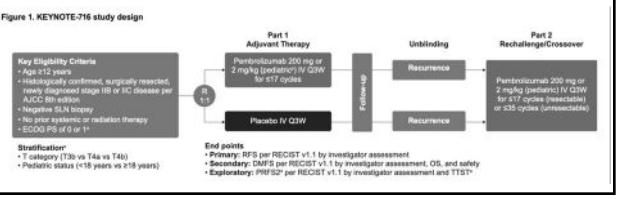

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Figure 2. Kaplan-Meier estimate of RFS in the overall population

	Events, n (%)	RFS, median (95% CI), months	HR (95% CI)
Pembrolizumab	149 (30.6)	NR (NR-NR)	0.62 (0.50-0.76)
Placebo	218 (44.6)	NR (59.1-NR)	

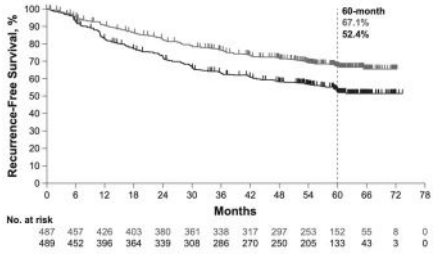

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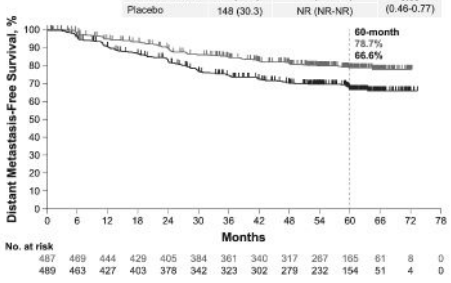
Figure 3. Kaplan-Meier estimate of DMFS in the overall population

	Events, n (%)	DMFS, median (95% CI), months	HR (95% CI)
Pembrolizumab	94 (19.3)	NR (NR-NR)	0.59 (0.46-0.77)
Placebo	148 (30.3)	NR (NR-NR)	



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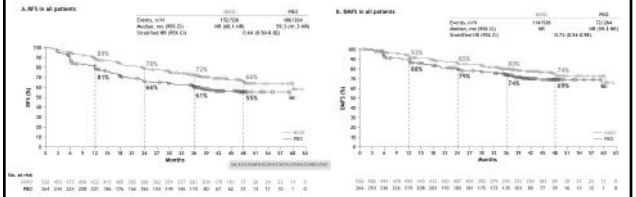
Adjuvant nivolumab vs placebo in resected stage IIB/C melanoma: 4-year update from CheckMate 76K

1610P



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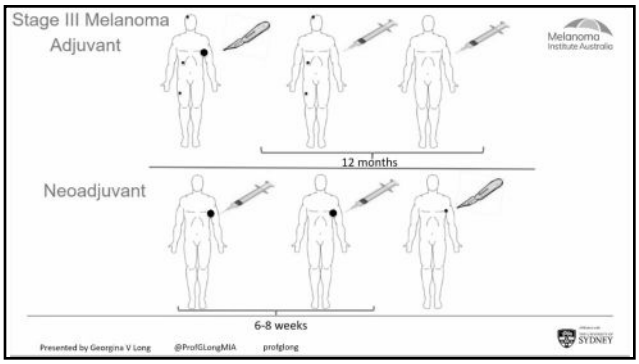

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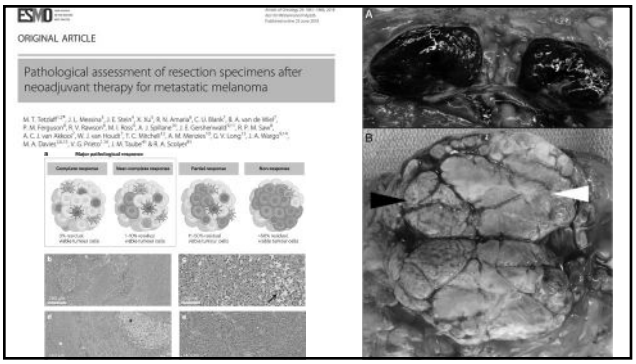

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SWOG 1801-Pembrolizumab
vs
NADINA study-Ipilimumab-Nivolumab
(reverse dose)

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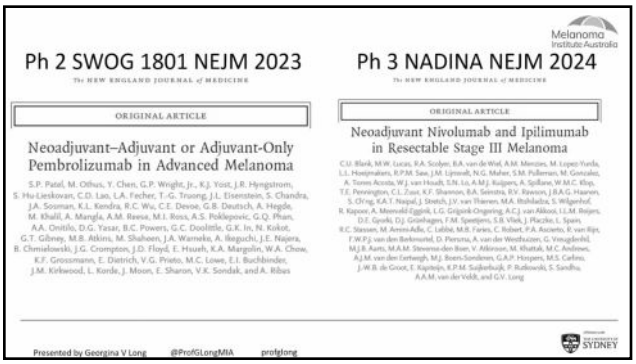

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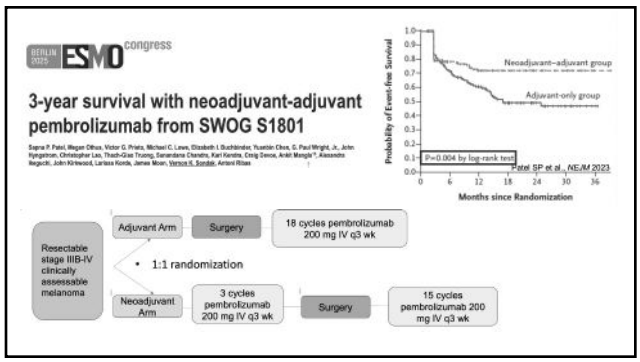

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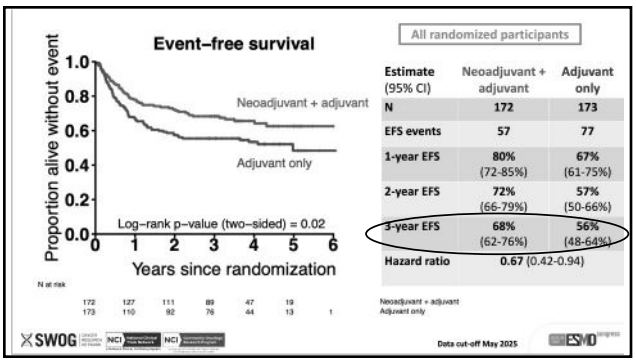

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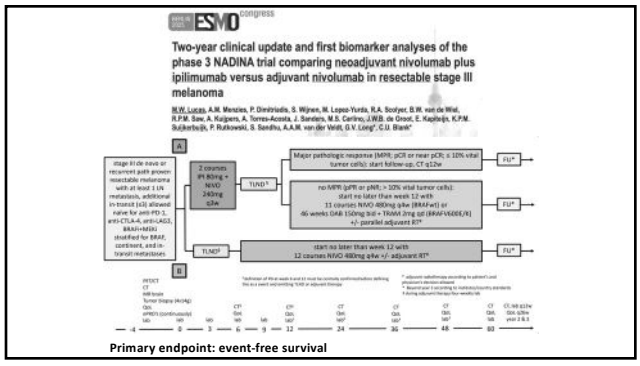

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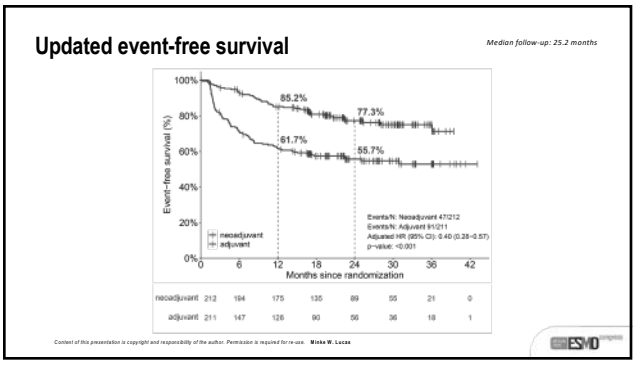

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NADINA – No Novel Safety Observations

	Neoadjuvant n=212	Adjuvant n=208
Any adverse event	204 (96.2%)	194 (93.3%)
Any grade ≥3 AE	100 (47.2%)	71 (34.1%)
Surgery related AE [1]	120 (60.6%)	151 (72.6%)
Surgery related grade ≥3 AE [1]	28 (14.1%)	30 (14.4%)
Systemic treatment related AE [2]	181 (85.4%)	123 (72.4%)
Systemic treatment related grade ≥3 AE [2]	63 (29.7%)	25 (14.7%)
Death due to treatment related AE	0	1 (0.5%)

[1] The surgery safety population included all patients that underwent surgery (neoadjuvant n=198, adjuvant n=208).
[2] The systemic treatment safety population included all patients that received at least one dose of systemic treatment (neoadjuvant n=212, adjuvant n=170).

Christian U. Blank, MD PhD

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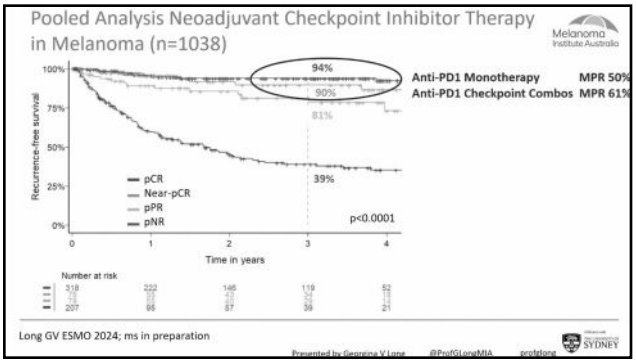

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Importance of dermatologists in F/U

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Conclusions

- **Melanoma Staging**
  - **Good diagnosis, good biopsy**
  - **AJCC classification: Breslow, ulceration, satellites**
  - **Nodal status: clinical or SLNB**
- **Types of melanoma treatments:**
  - **Metastatic: 50% MSS, new combo (Nivo-Rela: less toxic)**
  - **Adjuvant: decrease 10-15% RFS (Stages III and IIb/IIc)**
  - **Neoadjuvant in stage IIIb: decrease 20-25% EFS**
- **Key role of dermatologists: clinical F/U and imaging**

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