Immunotherapy for Non-Melanoma Skin Cancers (BCC, Squamous, & Merkel) and What After IO Failure?

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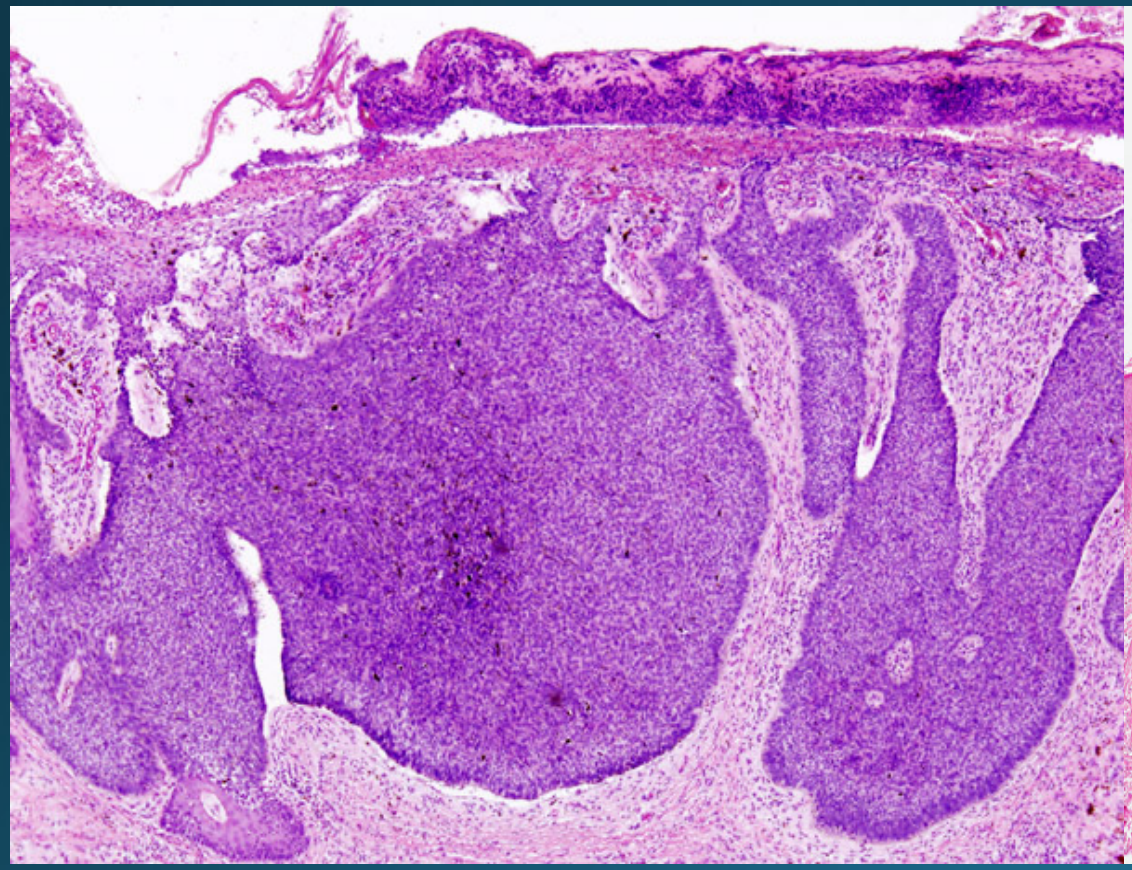
Outline

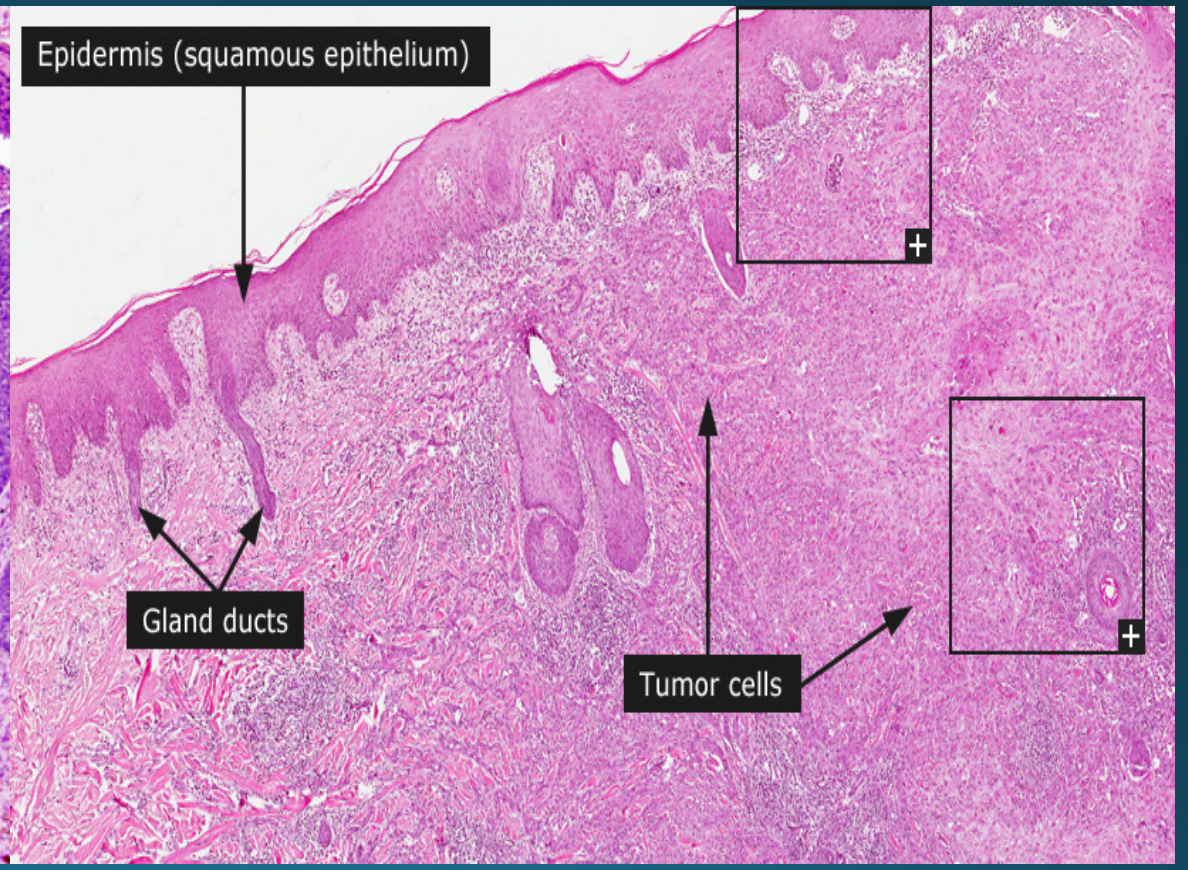
- Squamous-cell carcinoma
- Basal cell carcinoma
- Merkell cell cancer

Epidemiology

- Most common cancers.
- Risk factors include chronic sun exposure, advanced age, skin that is sensitive to UV radiation, and immunosuppression.
- More than 95% of patients are cured with surgery.
- Locally advanced disease can result in extensive morbidity through tissue destruction.
- Metastatic disease is considered incurable.

Histopathology





Characteristics and biologic behavior

- Tumor mutation burden is high because of chronic skin damage from UV light.
- Immune system surveillance is critical for preventing cancer in the immunocompetent.
- Patients who have a primary immuno-compromised system or those on immune-suppressive treatments are up 250 times more likely to get these cancers.

Cemiplimab in advanced cutaneous SCC

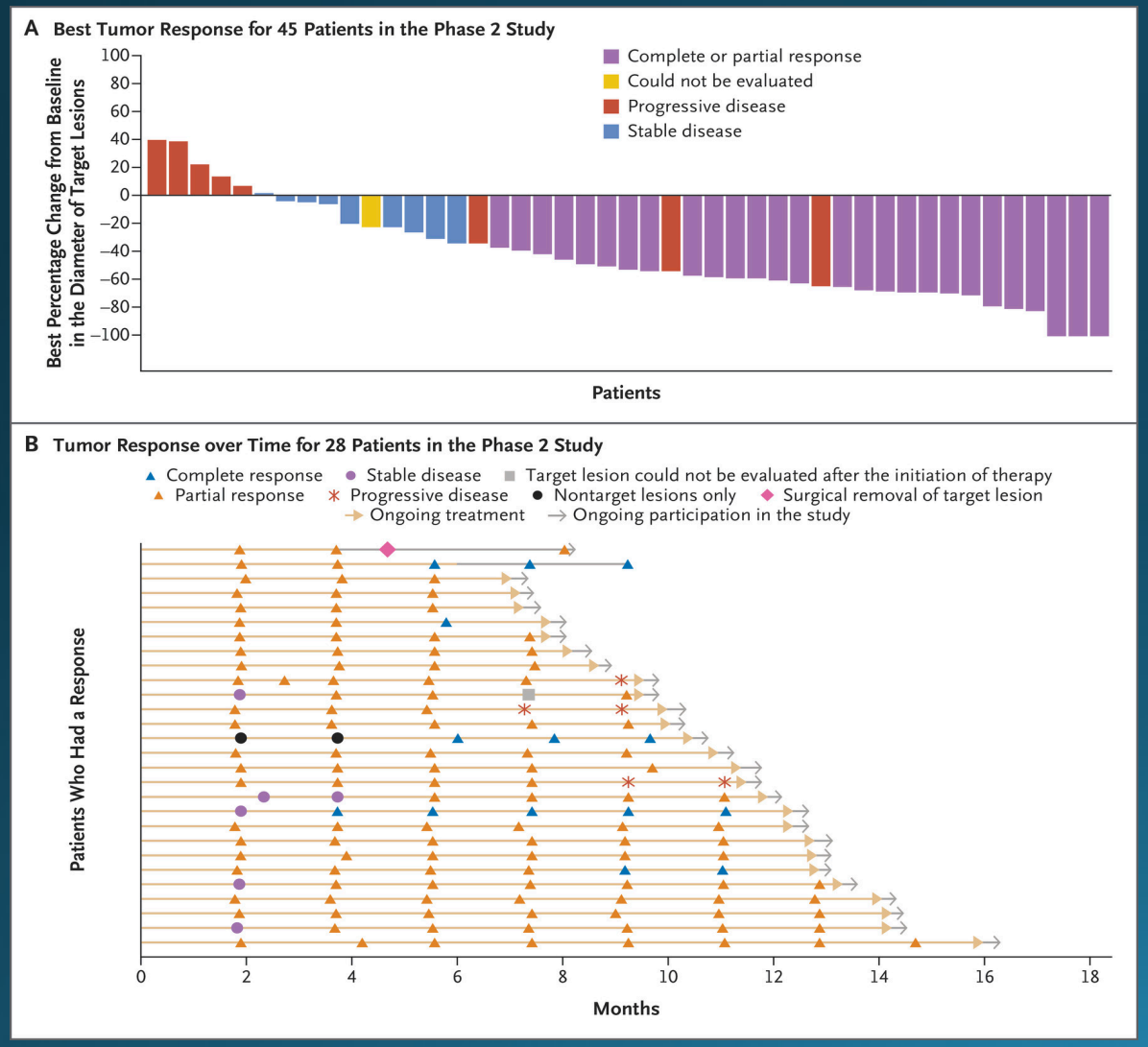
- 75 patients with locally advanced or metastatic cutaneous SCC.

- Cemiplimab 3mg/kg i.v. every 2 weeks.

*RR: 50%
*mTTR: 2.3mths
*DOR: 54% >6mths

NEJM 2018; 379: 341-351

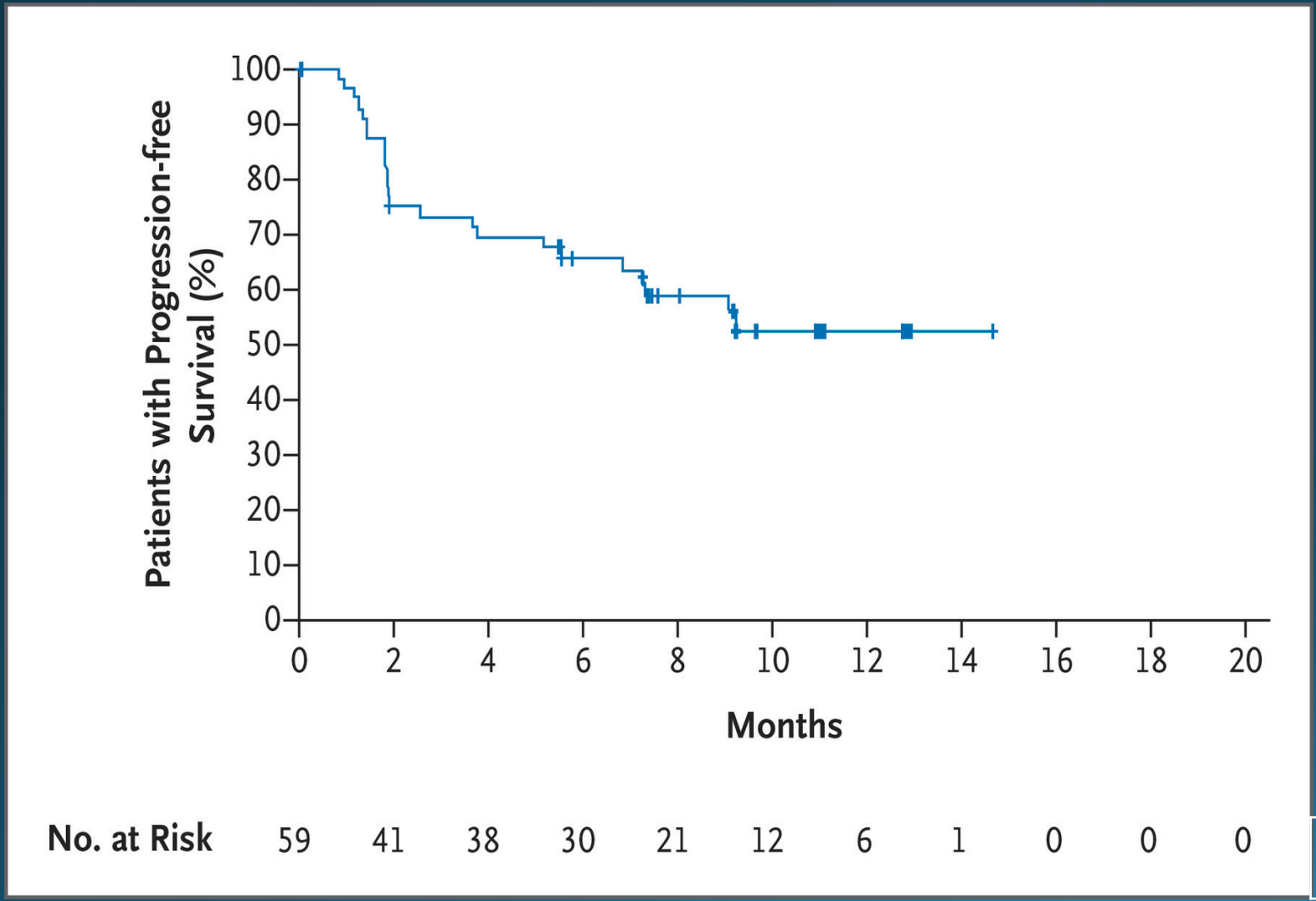
Cemiplimab in advanced cutaneous SCC



*23-28 (82%) patients who responded continued to respond at the time of data cutoff.

NEJM 2018; 379: 341-351

Cemiplimab in advanced cutaneous SCC



*PFS 53% at 12 months.
*OS 81% at 12 months.

NEJM 2018; 379: 341-351

Pembrolizumab in advanced cutaneous SCC

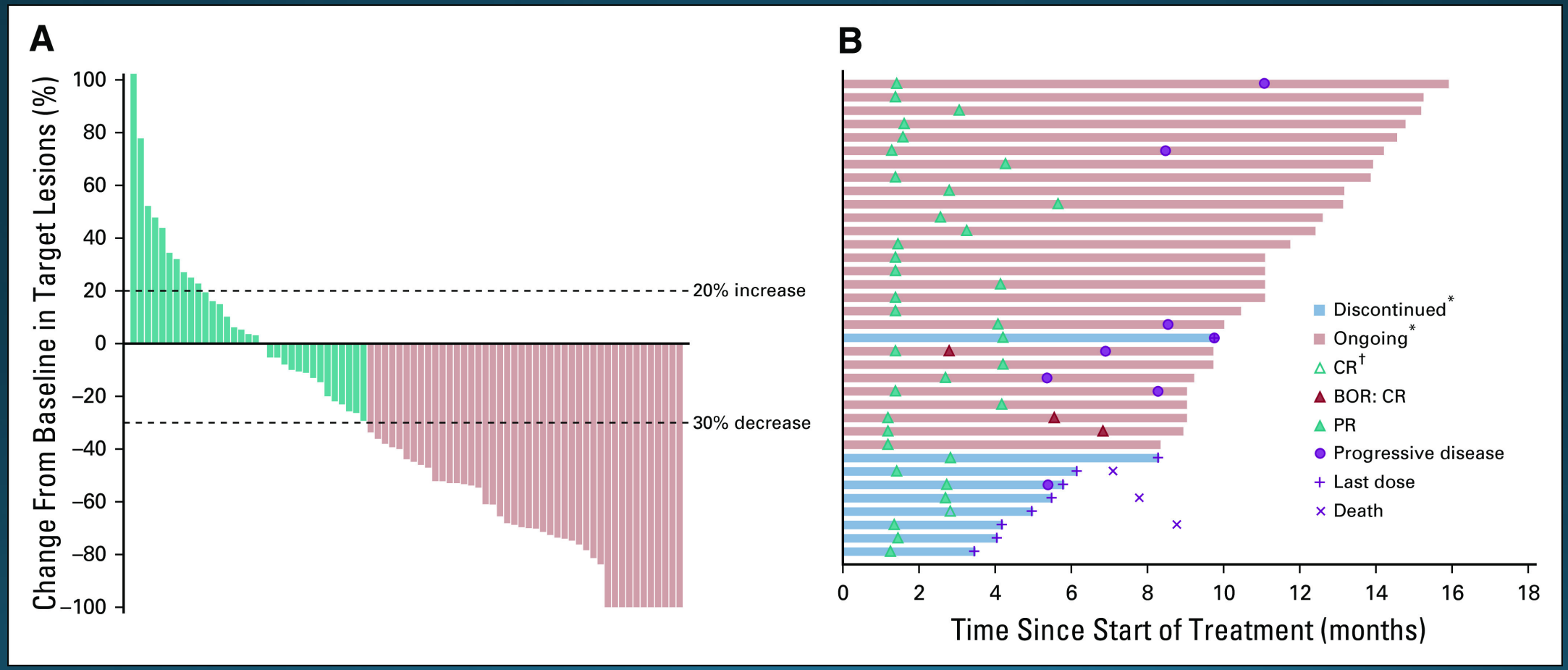
- 105 patients with locally advanced or metastatic cutaneous SCC.

- Pembrolizumab 200mg i.v. every 3 weeks.

*RR: 34%
*mTTR: 1.5mths

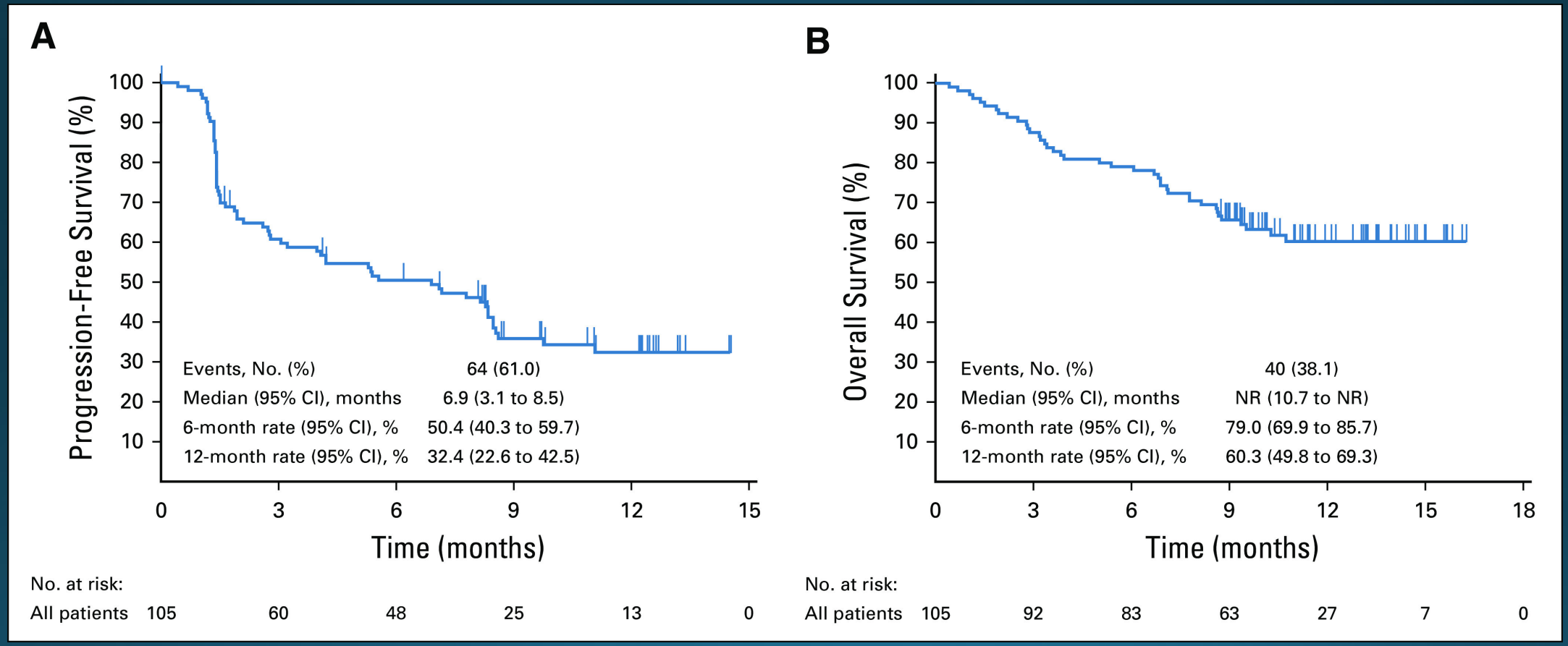
JCO 2020; 25: 2916-2925.

Pembrolizumab in advanced cutaneous SCC



JCO 2020; 25: 2916-2925.

Pembrolizumab in advanced cutaneous SCC



JCO 2020; 25: 2916-2925.

IGNYTE Phase 1/2

- 26 patients with locally advanced or metastatic cutaneous SCC.

RP1 intratumoral injection every 2 weeks for 8 doses plus nivolumab 240mg i.v. every 2weeks for 8 doses. Followed by nivolumab 480mg every 4 weeks for up 2 years.

- ORR: 60%
- CR: 46.6%
- mDOR: Not reached.

Niu J, et al. MH&NCS;abst 12:2/25/2022.

Cosibelimab in metastatic cutaneous SCC

- 78 patients with metastatic cutaneous SCC.

- Cosibelimab 800mg i.v. every 2 weeks.

- ORR: 47.4%
- CR: 8%
- PR: 40%
- mDOR: Not reached.
- 76% responses ongoing at 15 months.

JCO 40, 2022 (suppl 16; abstr 9537).

Immunotherapy followed by cetuximab in advanced cutaneous SCC: I-TACKLE trial.

- 43 patients with LA/M cutaneous SCC treated with pembrolizumab 200mg i.v. every 3 weeks.

In case of CR or PR ->pembrolizumab 200mg i.v. every 3 weeks.

In case of SD or PD ->cetuximab 400mg/sm i.v. loading dose then 200mg/sm weekly plus pembrolizumab 200mg i.v. every 3 weeks.

- 23 patients C+P
- ORR: 44%
- 1 year PFS: 42%
- Grade 3-4 TRAE 35%.
  *Dermatitis.

JCO 40, 2022 (suppl 16; abstr 9520).

Phase II trial of neoadjuvant immunotherapy for advanced resectable cSCC.

- 20 patients with advanced cutaneous SCC.

- Cemiplimab 350mg i.v. every 3 weeks for 2 doses prior to surgery.

- 85% achieved a pathologic response <50% viable tumor.
- 10% pPR >10-50%
- 20% mPR ,<10% viable tumor
- 55% pCR.

*Pts with pCR did not receive RT after surgery.

* At mFU of 34.5 months 100% of pts with pCR were alive.

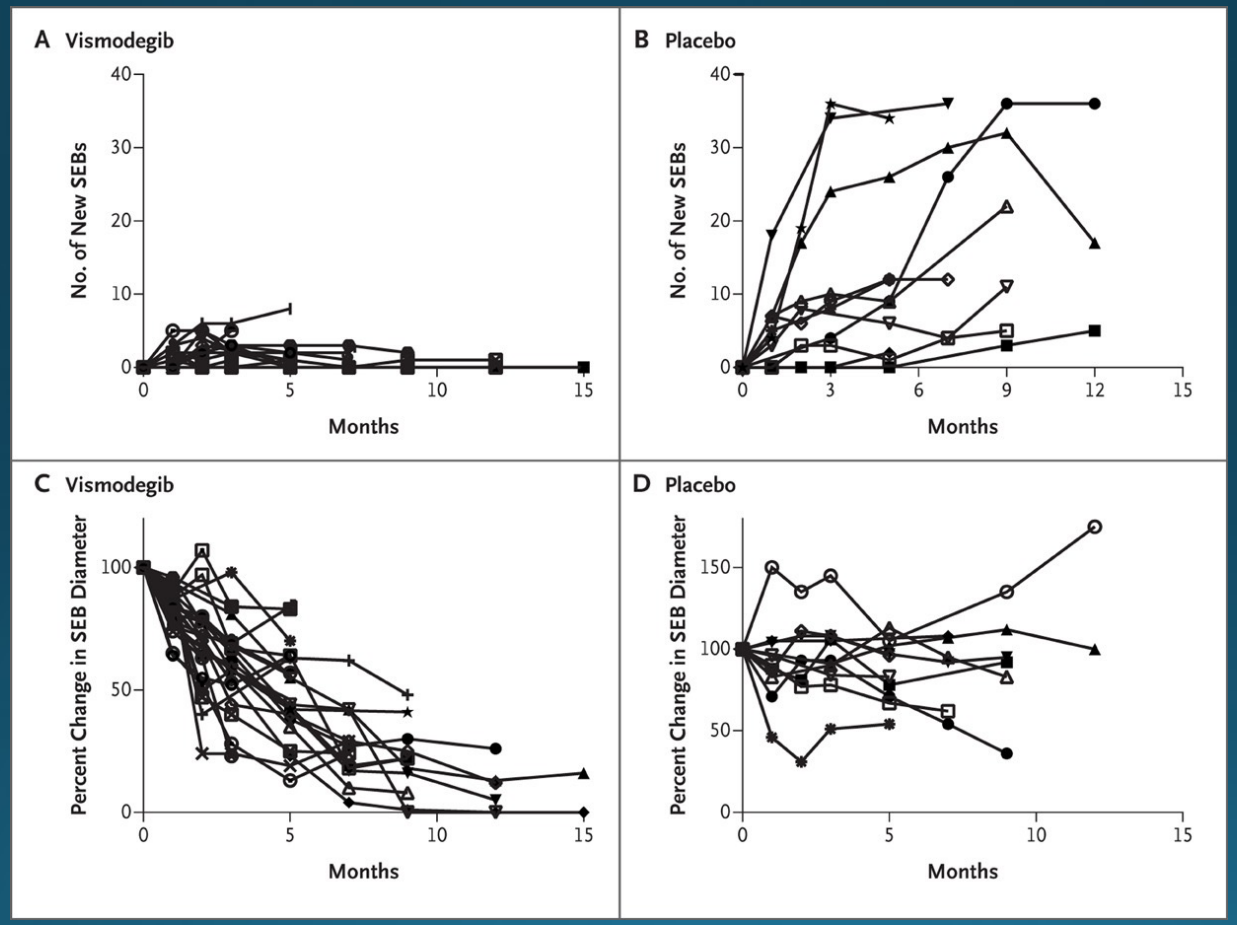
JCO 40, 2022 (suppl 16; abstr 9516).

Vismodegib for basal-cell nevus syndrome

Basal-cell nevus syndrome patients inherit a defective patched 1 (PTCH1) gene. Inhibits the hedgehog signaling pathway.

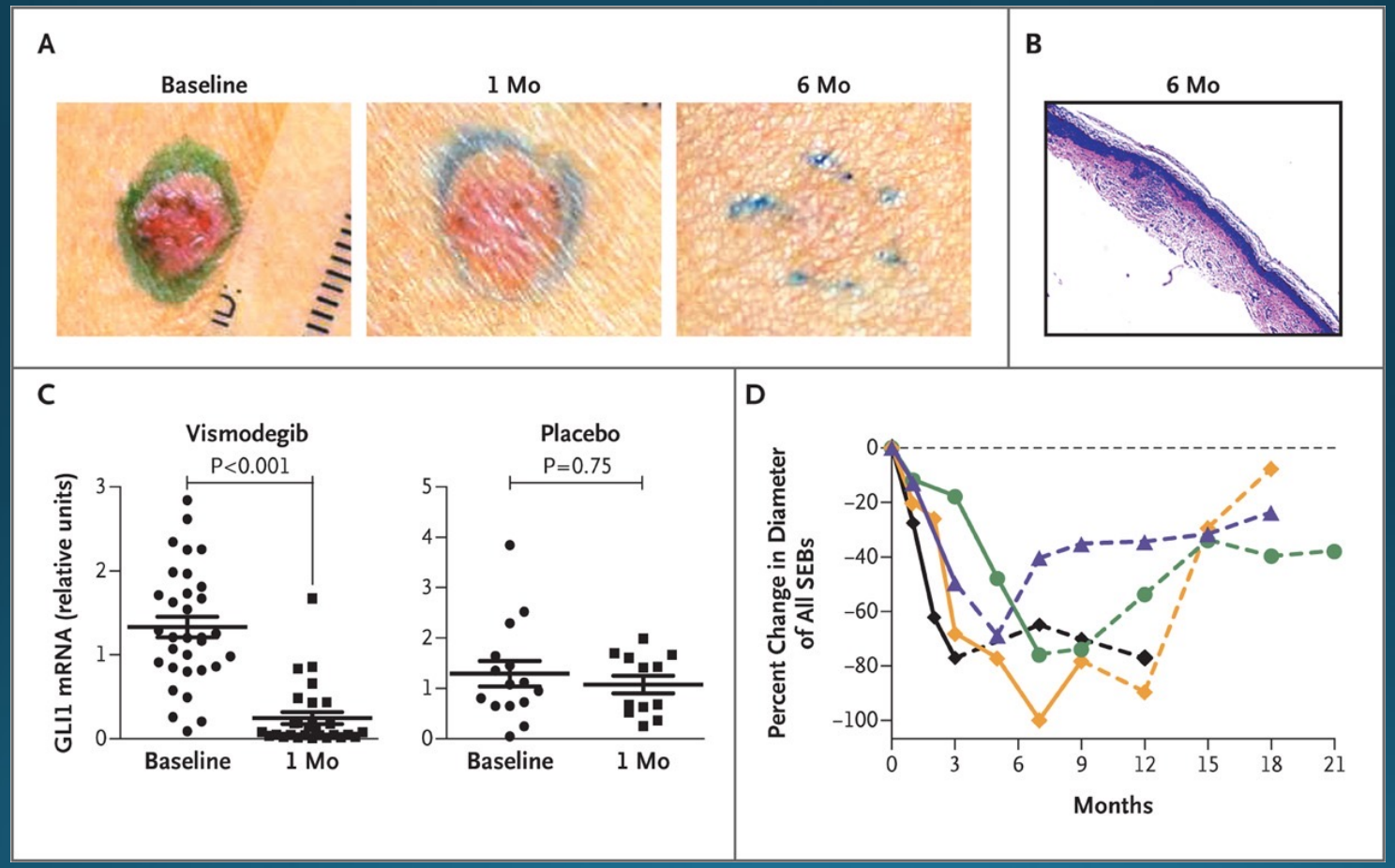
Vismodegib inhibits the hedgehog pathway.

Vismodegib for basal-cell nevus syndrome



NEJM 2012; 366: 2181-2188.

Vismodegib for basal nevus syndrome

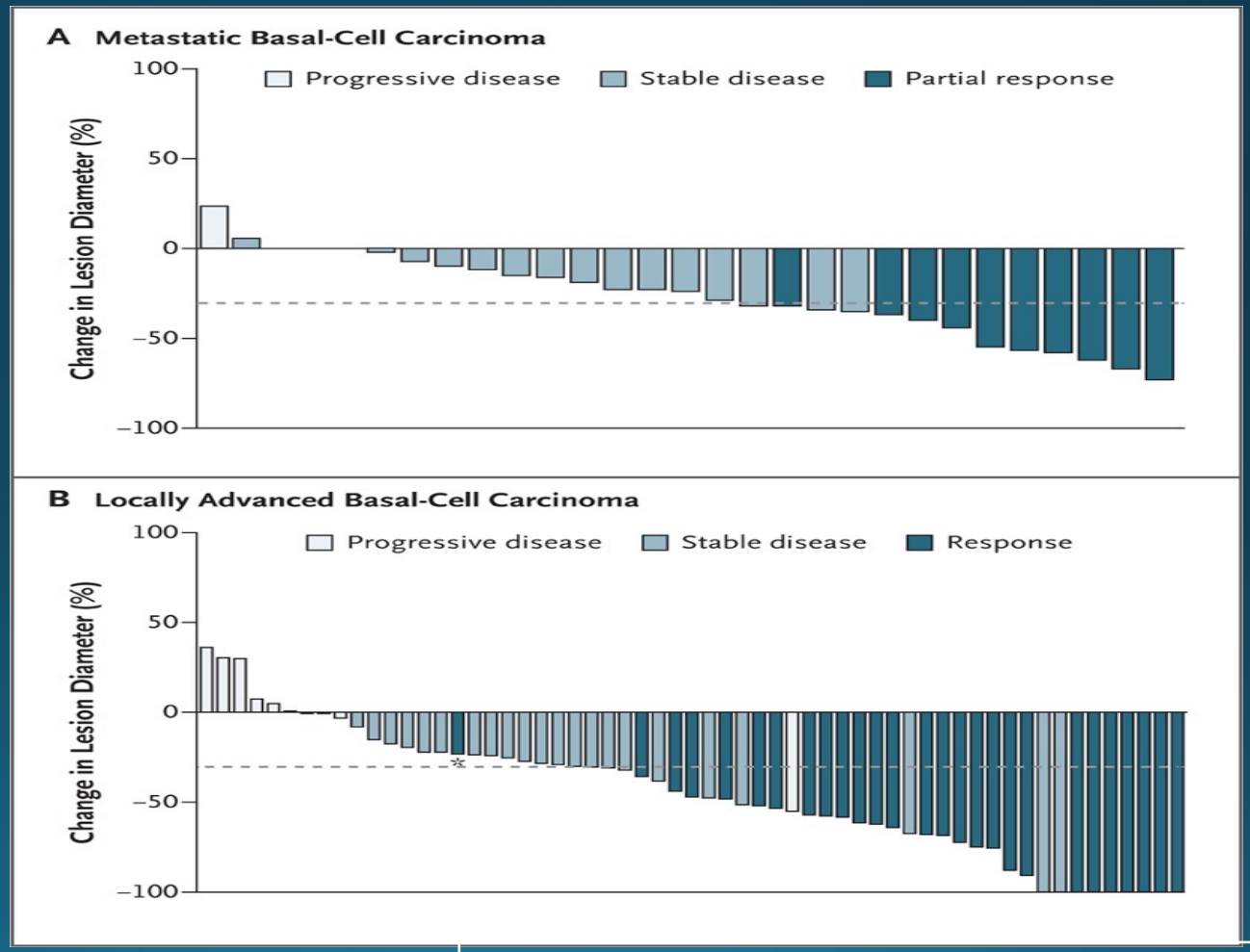


NEJM 2012; 366: 2181-2188.

Vismodegib for basal-cell carcinoma

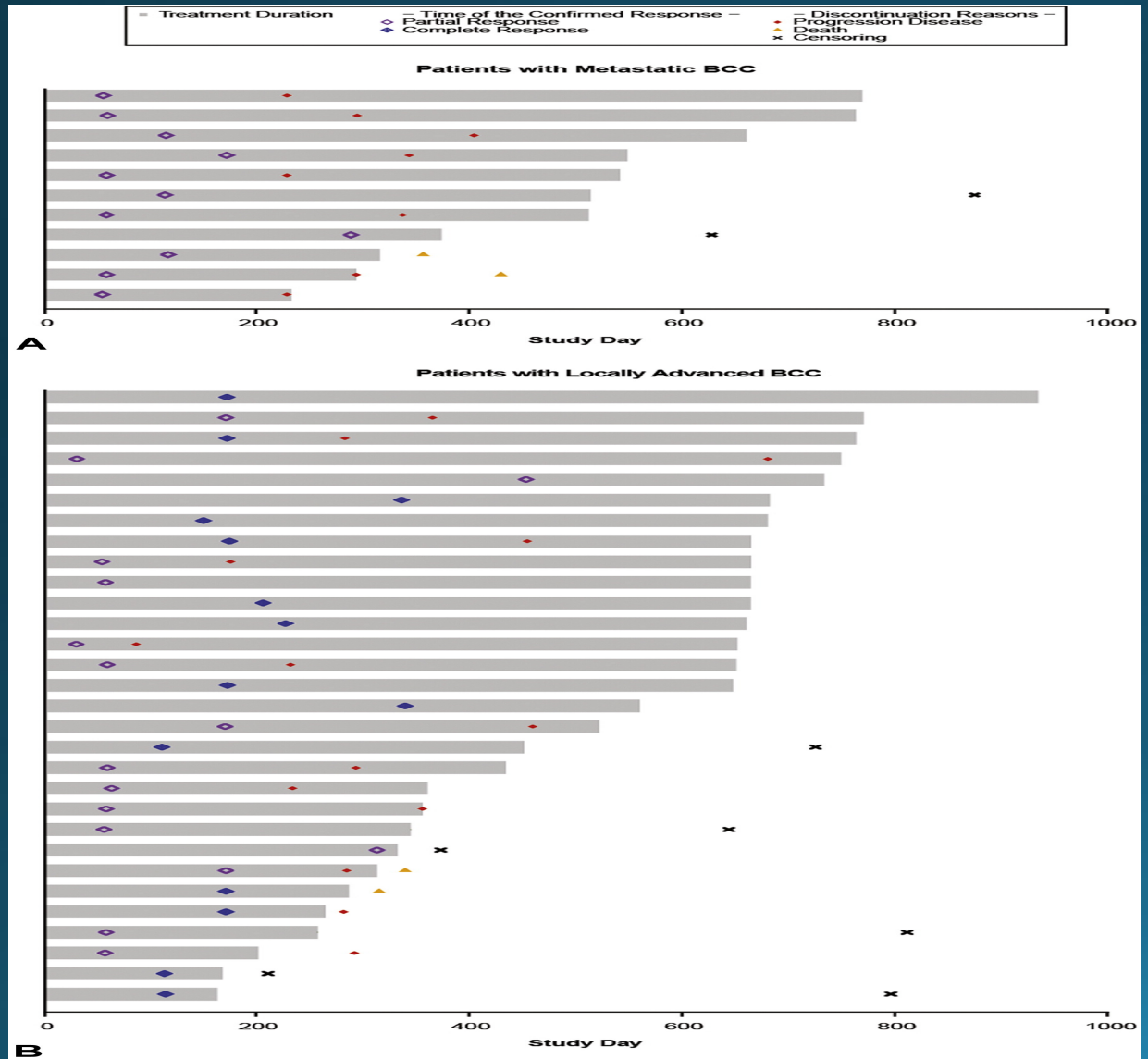
- 99 pts with locally advanced or metastatic disease.

Vismodegib 150mg P.O daily.



NEJM 2012; 366: 2171-2179.

Vismodegib for basal-cell carcinoma



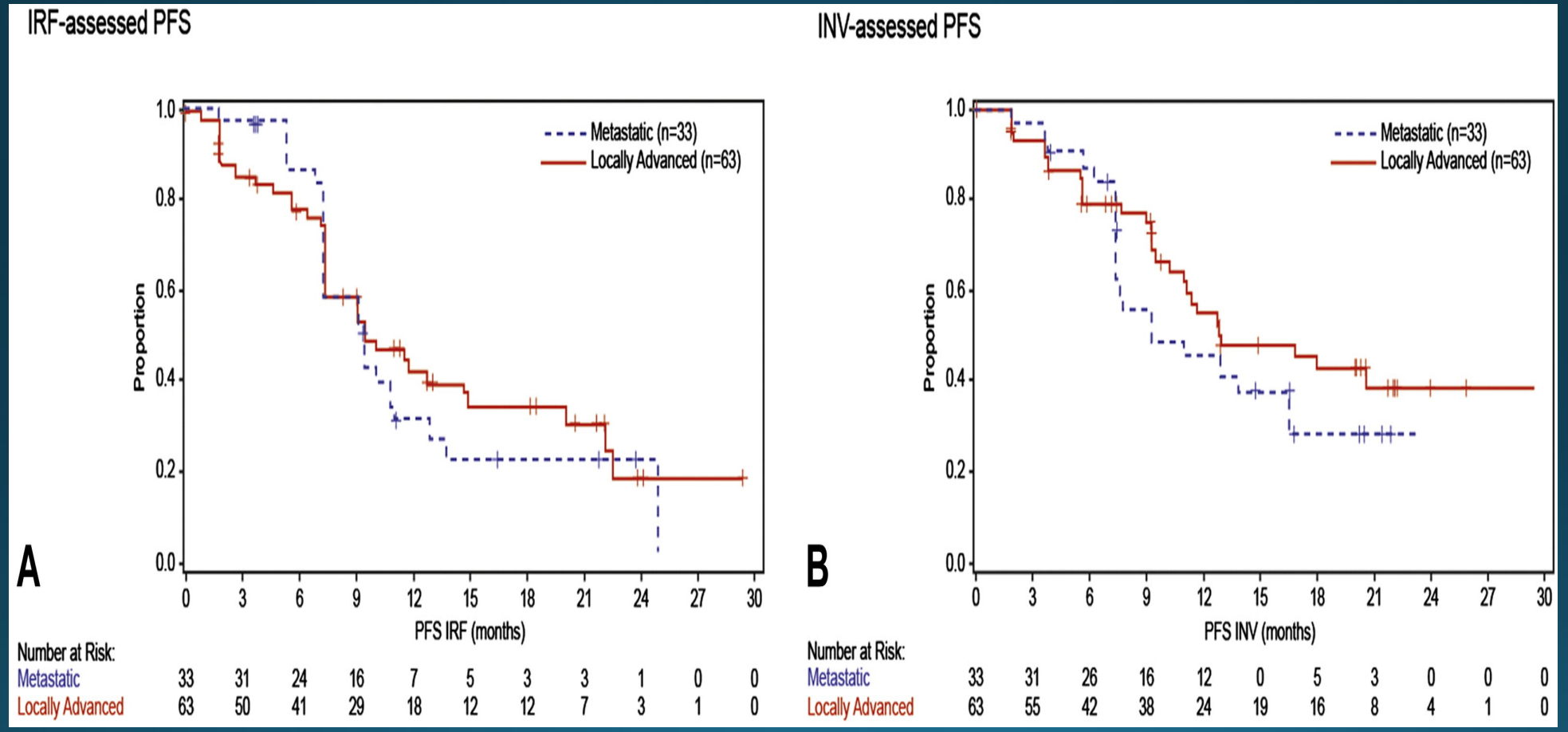
*RR: 33%

*DOR: 9.5mths

*RR: 47%

JAAD 2015; 72: 1021-1026.

Vismodegib for basal-cell carcinoma



JAAD 2015; 72: 1021-1026.

Sonidegib for basal-cell carcinoma

- BOLT trial

230 patients with locally advanced or metastatic cutaneous BCC.

- 1:2 randomization

Sonidegib 200mg P.O. daily

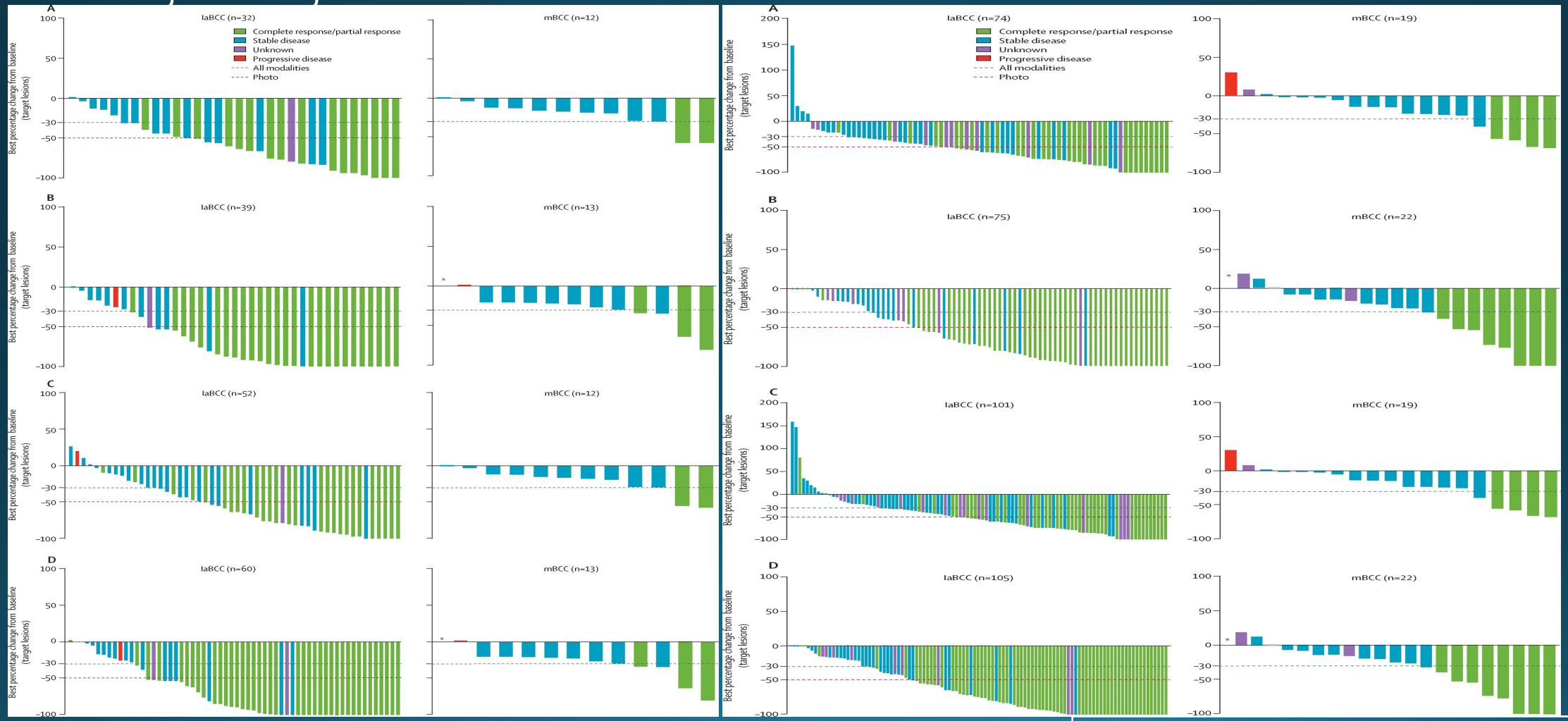
Sonidegib 800mg P.O. daily

Lancet Oncol 2015; 16: 716-728.

Sonidegib for basal-cell carcinoma

Sonidegib 200mg

Sonidegib 800mg



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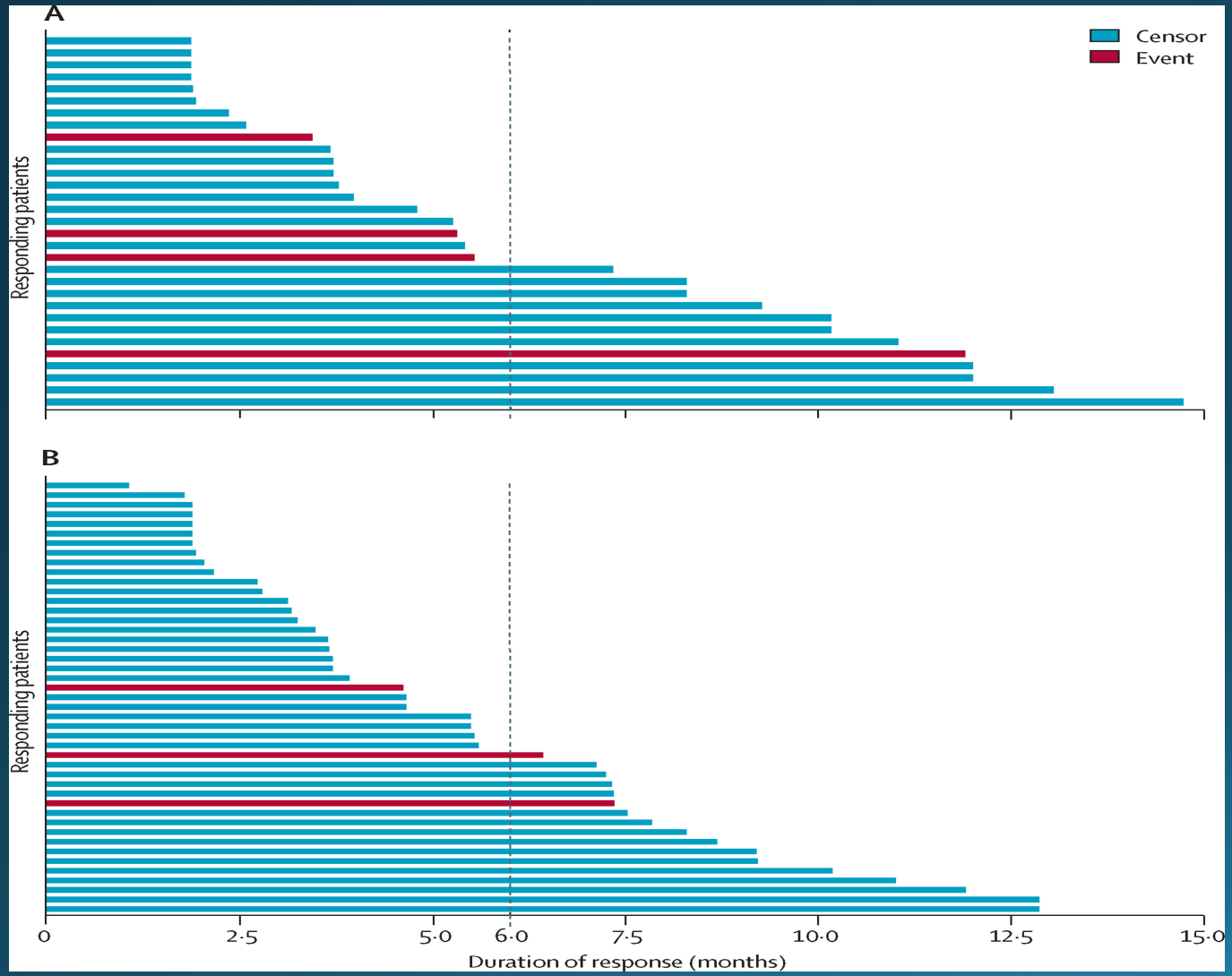
Sonidegib for basal-cell carcinoma



	200mg	800mg
• ORR:	58%	55%
• Dx. Red:	32%	60%
• Tx. Disc:	22%	33%
• Gd 3-4 AE:	14%	30%

Lancet Oncol 2015; 16: 716-728.

Cemiplimab for BCC after progression to HHIS.

- 28 patients with locally advanced or metastatic BCC after progression or intolerance to HHIS.

Cemiplimab 350MG i.v. every 3 weeks.

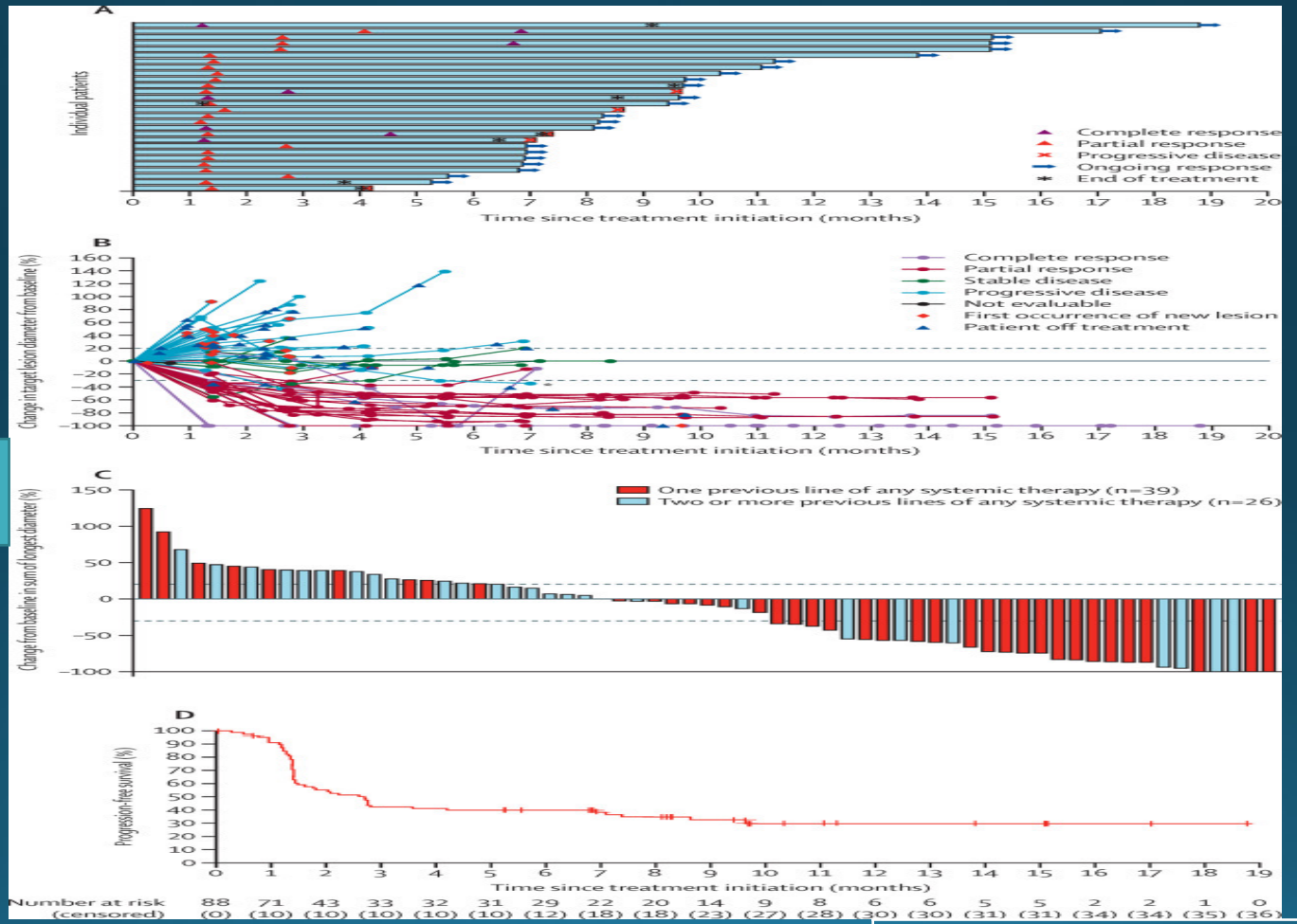
*RR: 28.6%
*mTTR: 3.2 months
*DOR: 9-23 months
*PFS: 8.3 months
*OS: 25.7 months

J Immunother Cancer 2020;8(Suppl3): A428.

Avelumab for chemotherapy refractory Merkel cell carcinoma.

- 88 pts with chemotx refractory disease.

- Avelumab 10mg/kg i.v. q 2 wks.

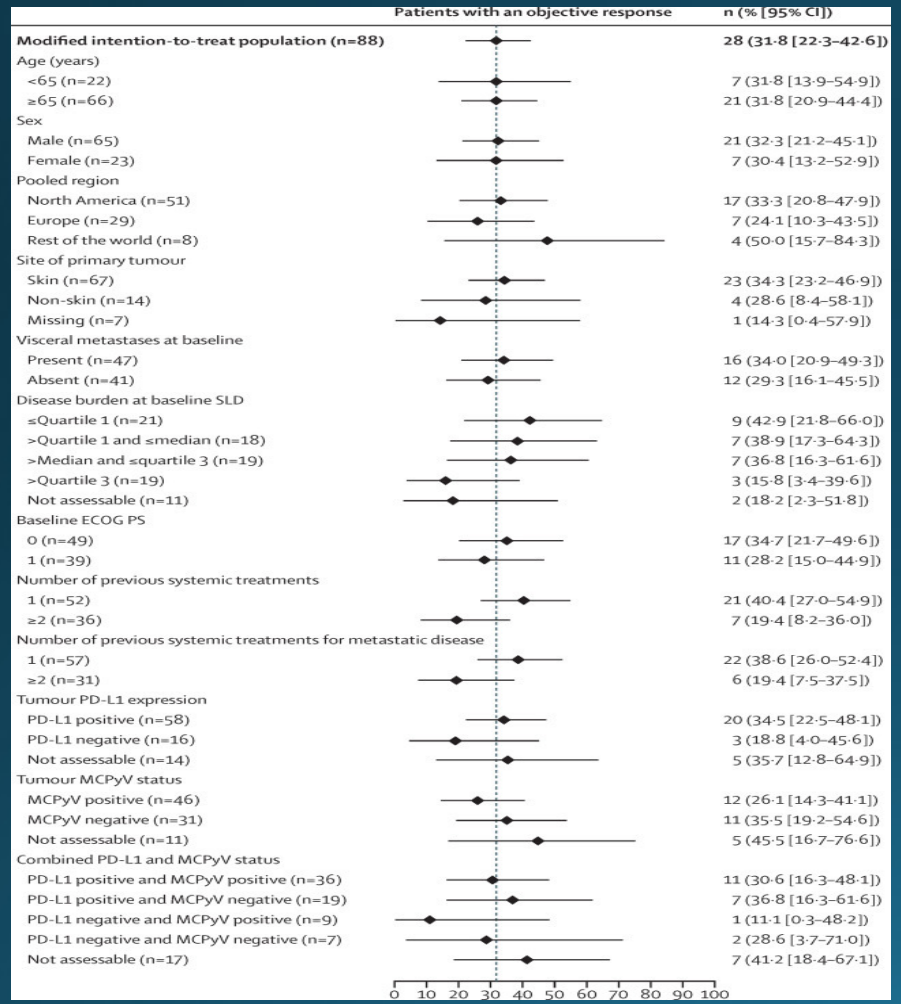


- ORR 28pts
- CR 8 pts
- PR 20 pts
- SD 9 pts

- PFS 2.7 months
- OS 11.3 months

Lancet Oncol 2016; 17: 1374-1385.

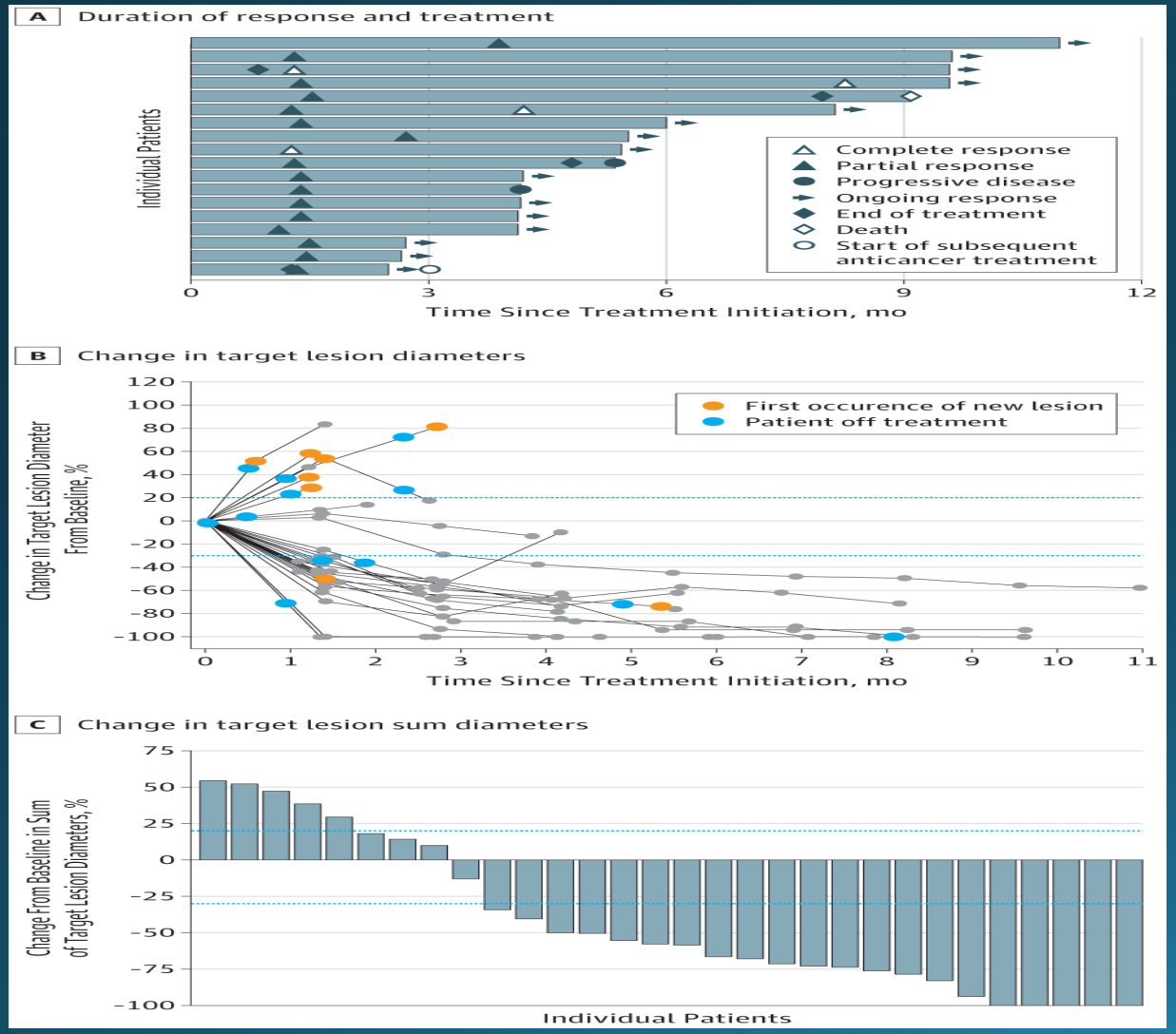
Avelumab for chemotherapy refractory Merkel cell carcinoma.



Responses were irrespective of PD-L1 expression or Merkel cell polyomavirus status.

Lancet Oncol 2016; 17: 1374-1385.

Avelumab for chemotherapy refractory Merkel cell carcinoma.



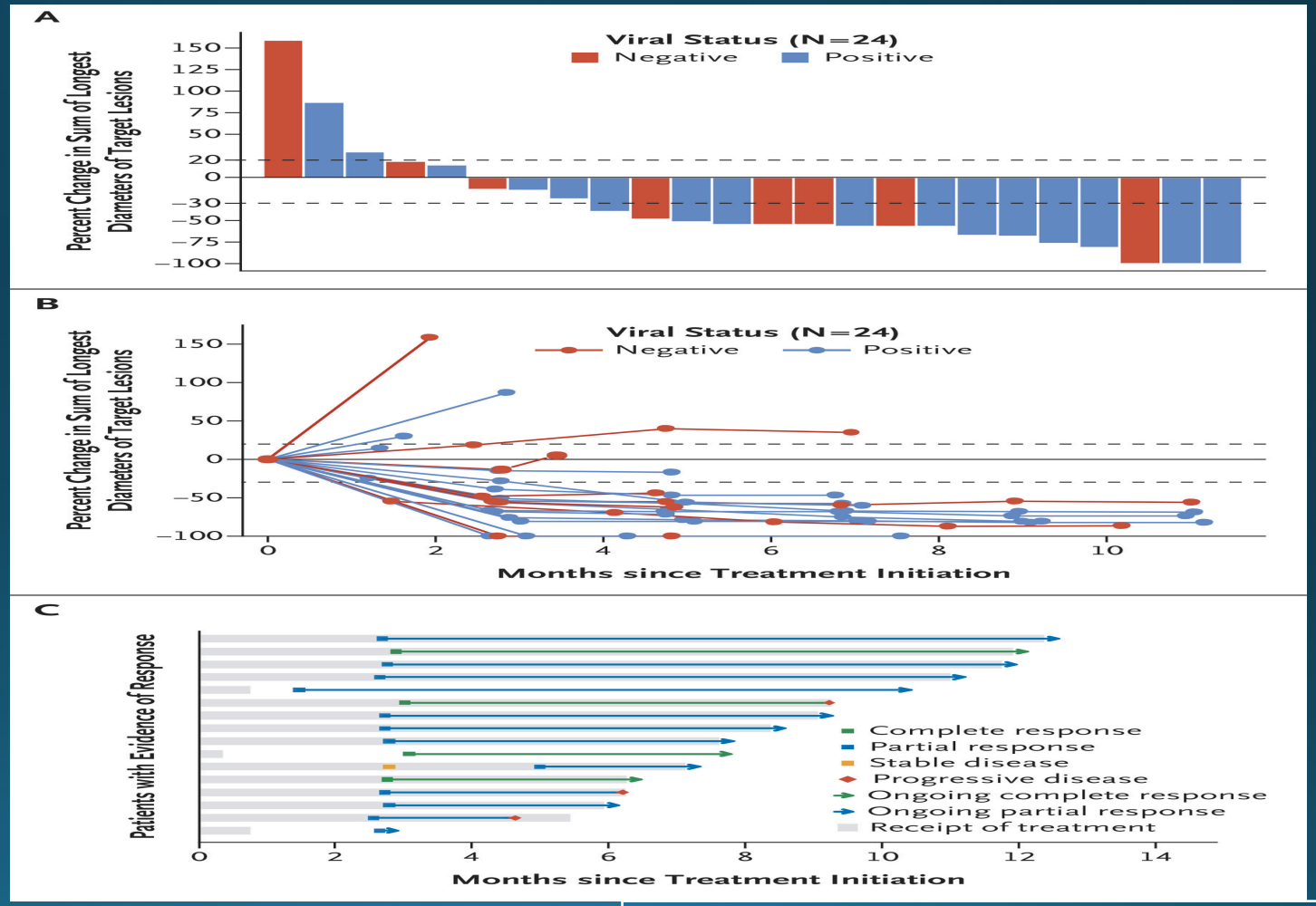
- PFS at 6 months: 40%
- OS at 6 months: 69%

Lancet Oncol 2016; 17: 1374-1385.

Pembrolizumab in advanced Merkel cell carcinoma treatment naïve.

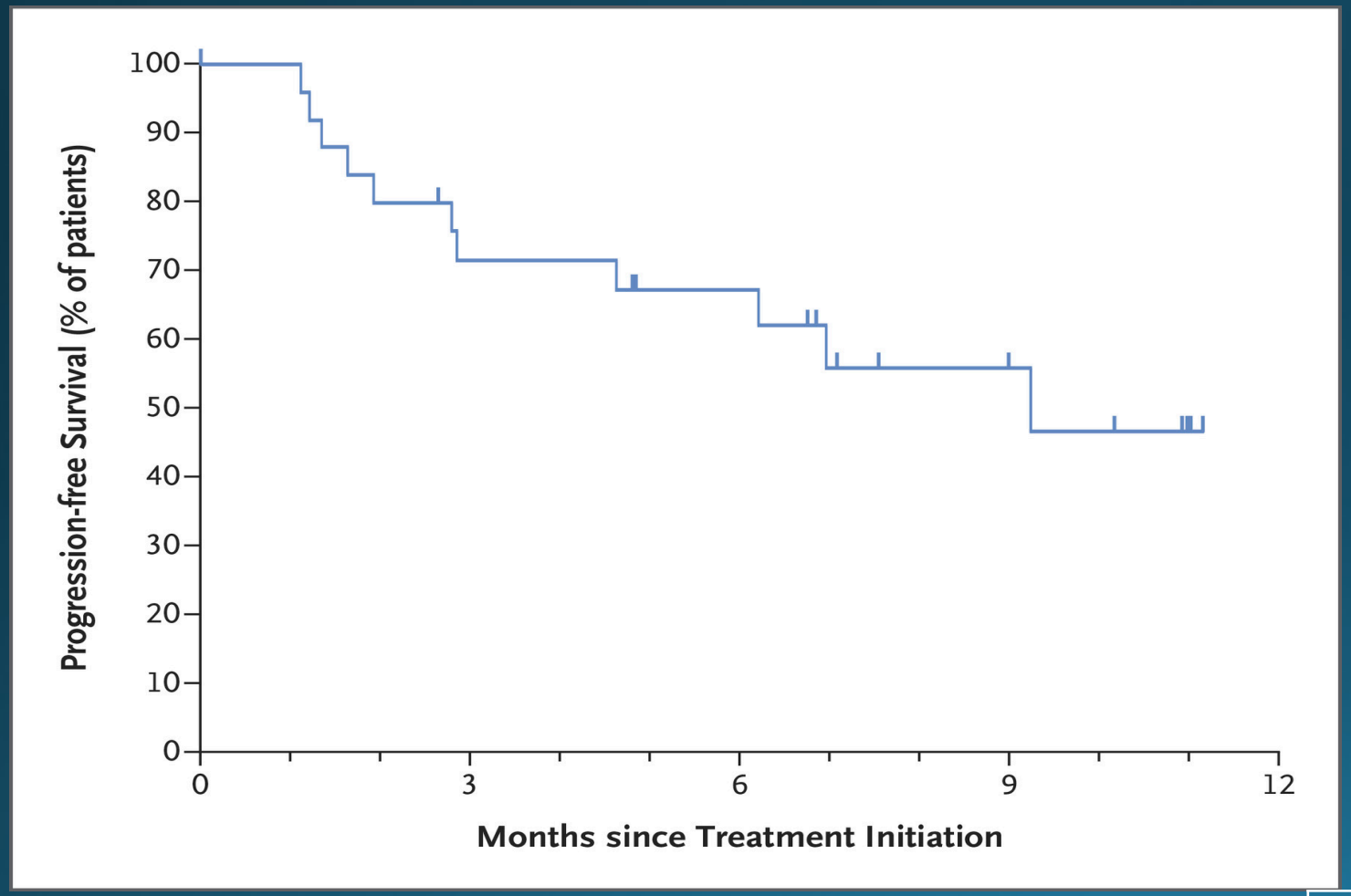
- 26 pts with chemotx naïve MCC.

Pembrolizumab 2mg/kg i.v. q 3 wks.



NEJM 2016; 374: 2542-2552.

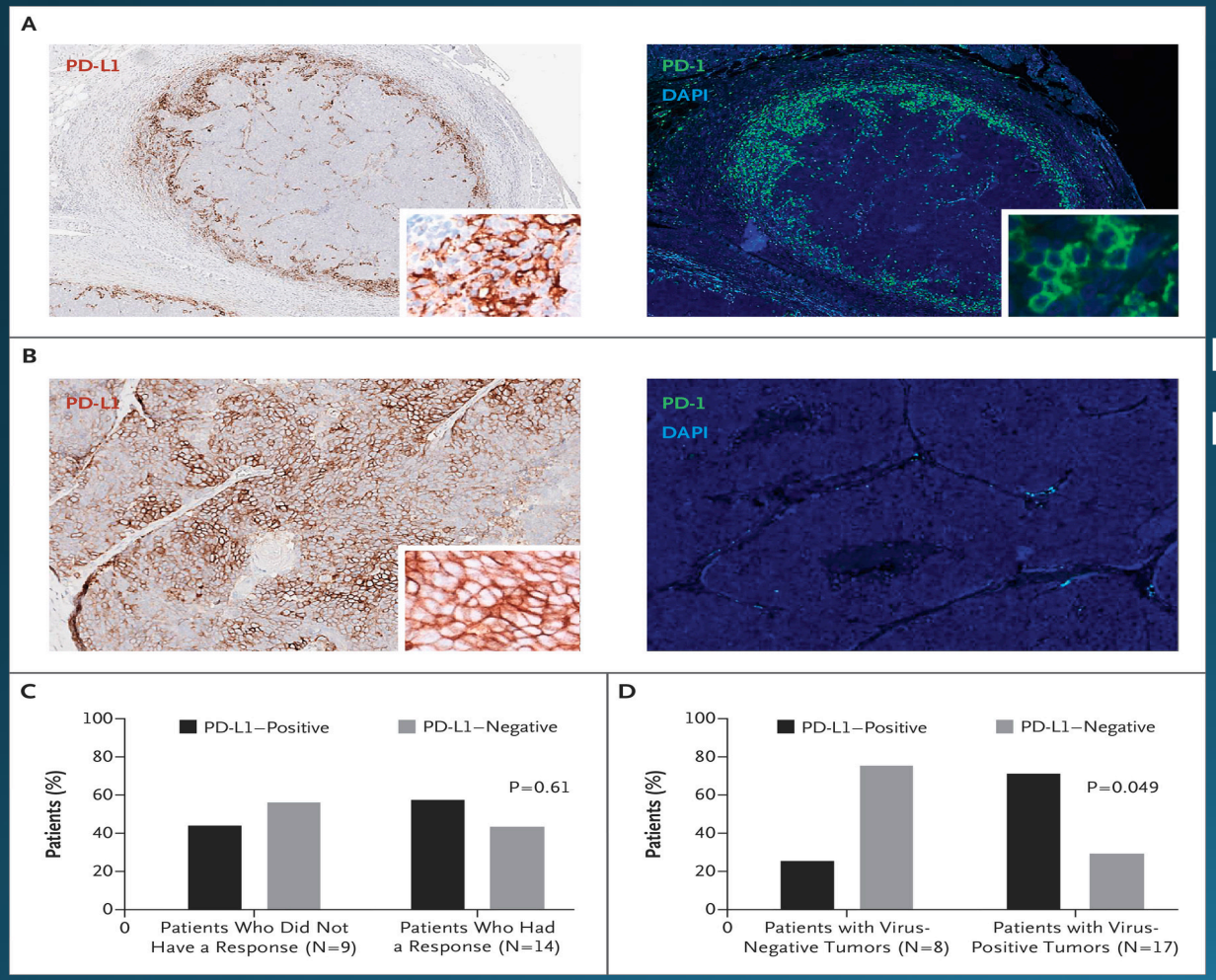
Pembrolizumab in advanced Merkel cell carcinoma treatment naïve.



- ORR 56%
- CR 4 pts
- PR 10 pts
- SD 1 pt

NEJM 2016; 374: 2542-2552.

Pembrolizumab in advanced Merkel cell carcinoma treatment naïve.



Responses were irrespective of PD-L1 expression or Merkel cell polyomavirus status.

NEJM 2016; 374: 2542-2552.

Phase 1b/2 navtemadlin after failure immunotherapy in MCC.

- 29 patients with TP53 wild-type MCC.

180mg dose selected for further evaluation.

- ORR: 25%
- DCR: 63%
- mTRR: 4.1 months
- SD 1 pt
- Grade 3-4 TRAE 68%. *Cytopenias.

JCO 40, 2022 (suppl 16; abstr 9506).