MESA 6: MELANOMA

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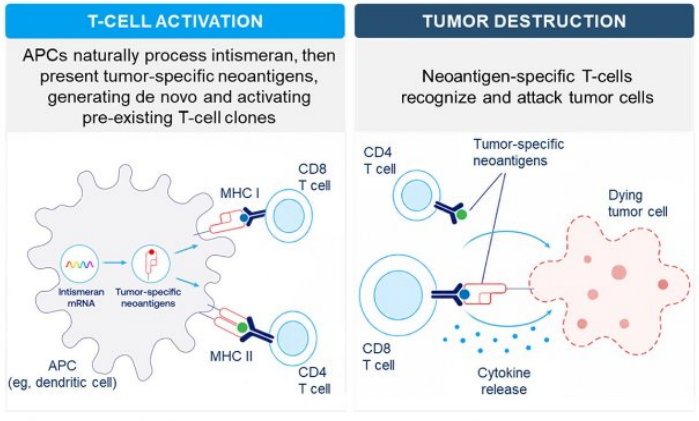
2026 ASCO ANNUAL MEETING

Individualized Neoantigen Therapy Intismeran Autogene Plus Pembrolizumab in Resected Melanoma: 5-Year Update of the KEYNOTE-942 Study



Randomized, phase 2, open-label study of adjuvant therapy in patients with completely resected melanoma at high risk of recurrence

Key eligibility criteria

- Age ≥18 years old
- Resected stage IIIB,[a] IIIC, IIID, or IV cutaneous melanoma
- Complete surgical resection within 13 weeks before first pembrolizumab dose
- Disease free at study entry
- ECOG PS score 0 or 1
- Tissue available for NGS

2:1 randomization

Stratified by disease stage[b]

Intismeran plus pembrolizumab (n=107)

Intismeran 1 mg IM Q3W × up to 9 doses

Pembrolizumab 200 mg IV Q3W × up to 18 doses

Pembrolizumab monotherapy (n=50)

Pembrolizumab 200 mg IV Q3W × up to 18 doses

Primary endpoint

- RFS

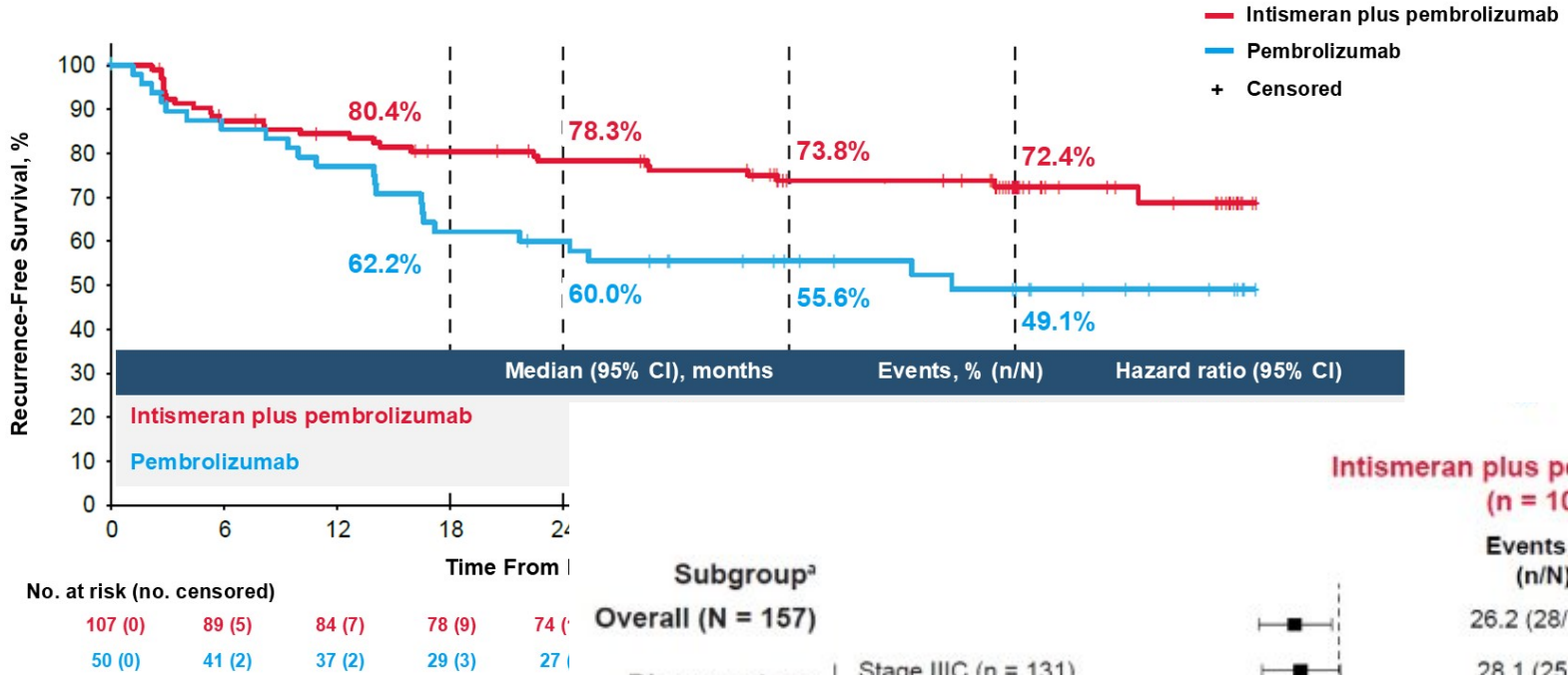
Secondary endpoints

- DMFS
- Safety

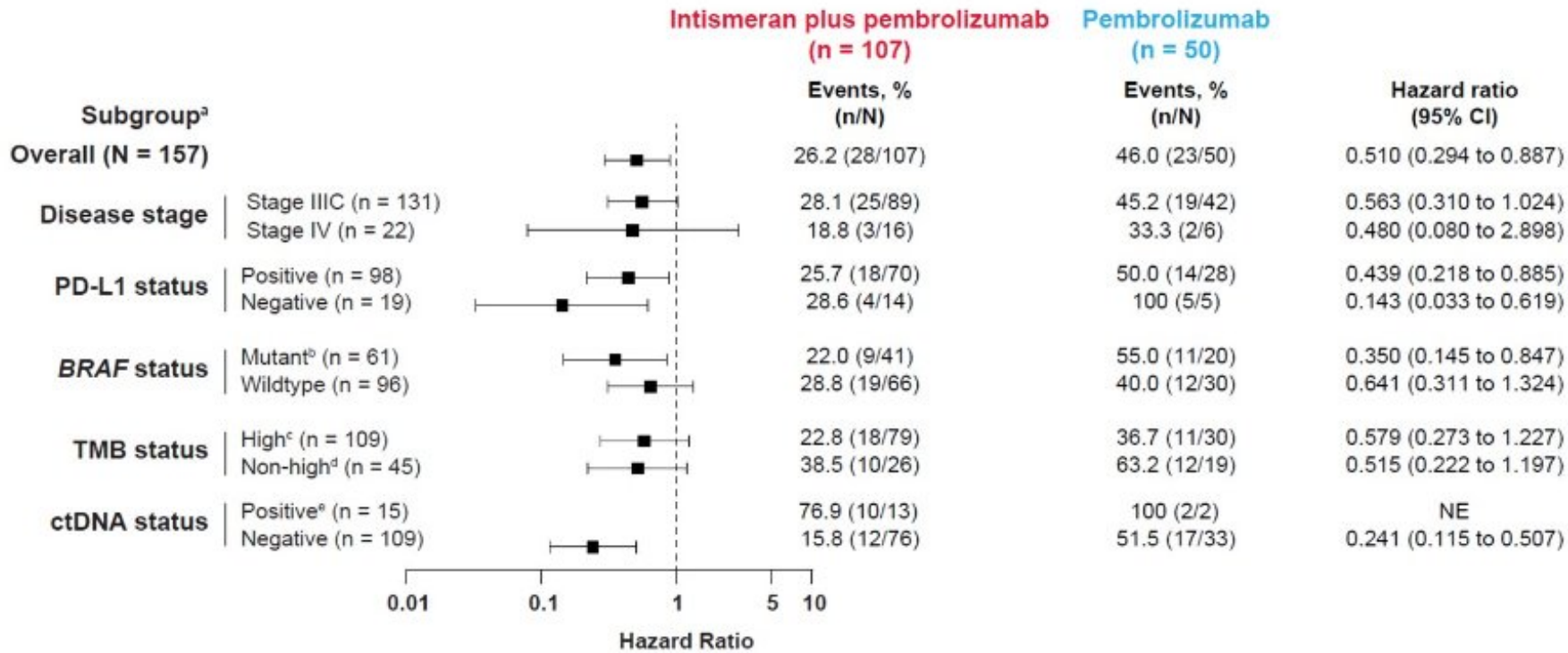
Exploratory endpoints

- OS
- Potentially predictive biomarkers
- Antigen-specific T-cell responses

Durable benefit in RFS (primary endpoint)



NE, not estimable.



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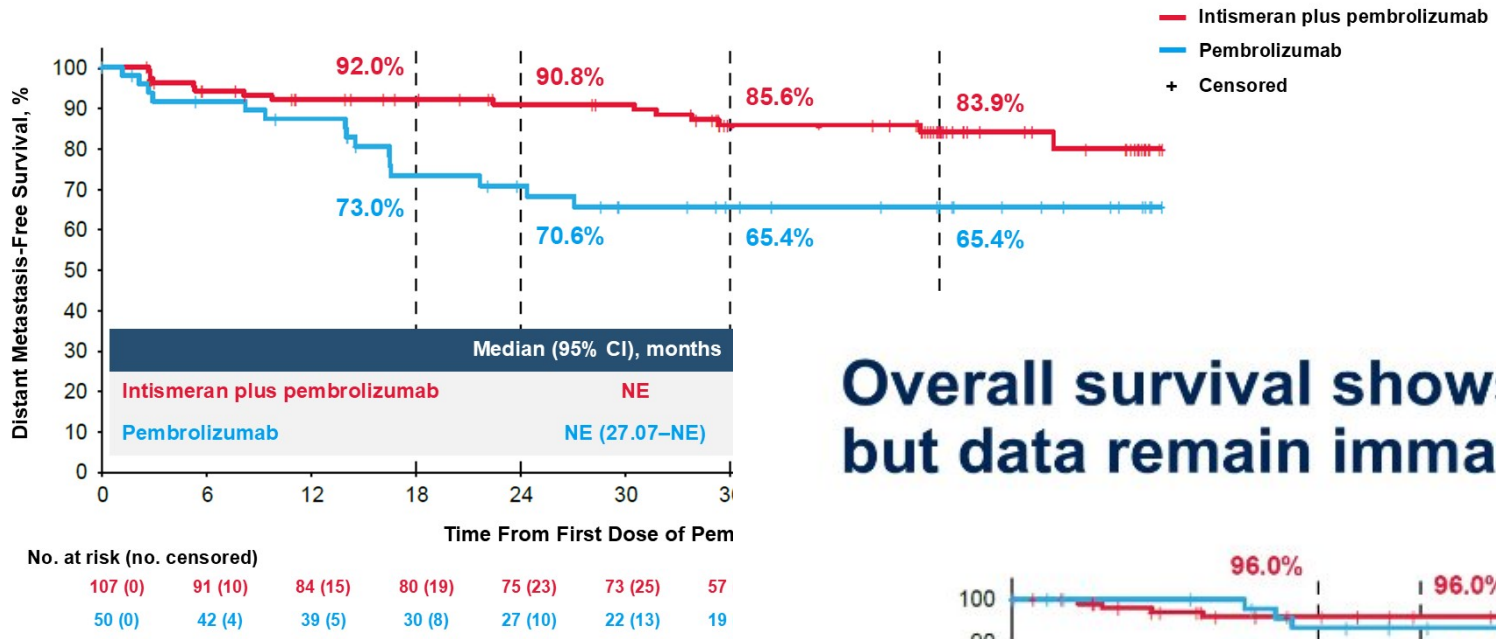
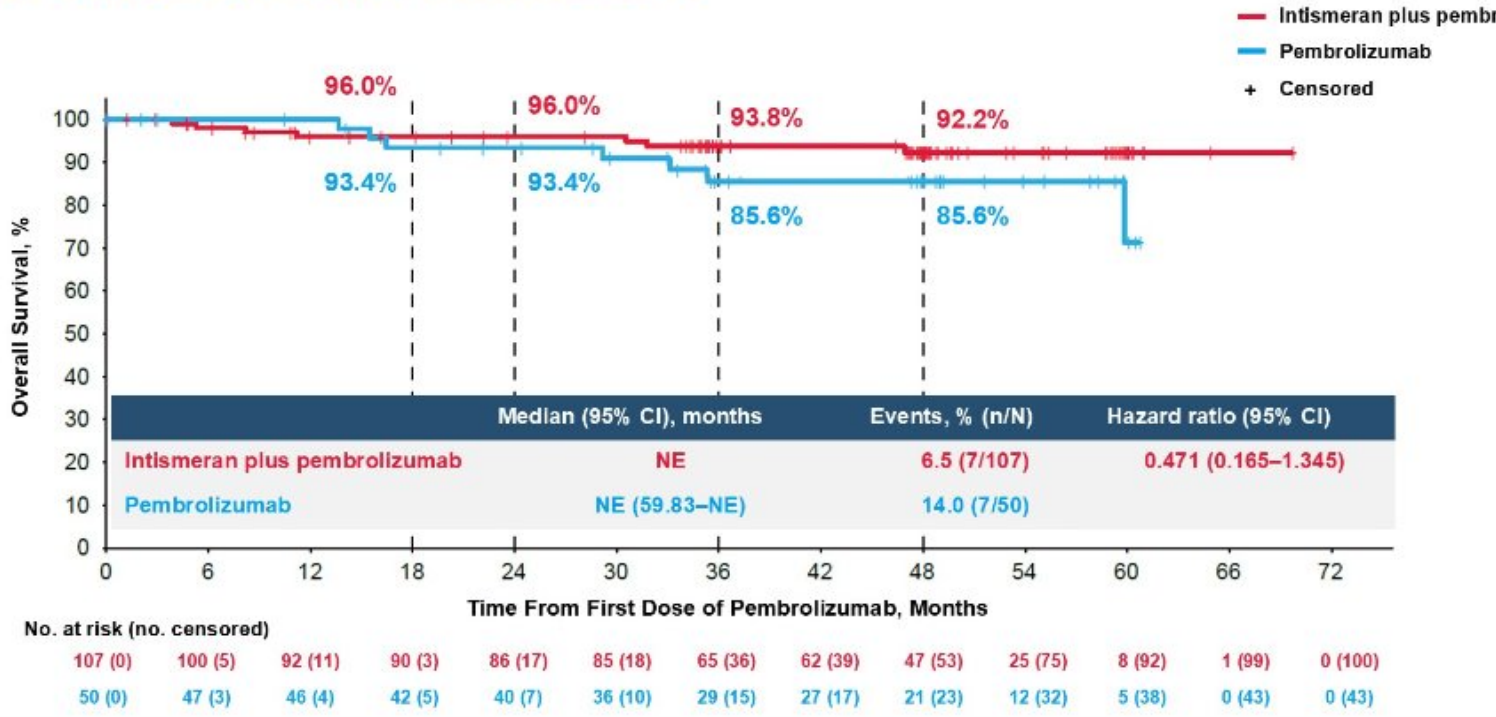
Durable benefit in DMFS (secondary endpoint)



PRESENTED BY: Matteo S. Carlino, MD, PhD

Overall survival shows an encouraging trend, but data remain immature



Conclusions

- Intismeran plus pembrolizumab demonstrated **durable and clinically significant improvements in RFS and DMFS** vs standard-of-care pembrolizumab in high-risk resected melanoma at 5 years of follow-up
  - 49% reduction in risk of recurrence or death and 59% reduction in distant metastasis or death
  - Encouraging trend in overall survival

- Intismeran plus pembrolizumab maintained a **manageable safety profile** without potentiation of immune-related AEs vs pembrolizumab monotherapy

- Intismeran plus pembrolizumab generated **sustained novel T-cell clonotype expansion,** which was associated with lack of recurrence, supporting a durable immune surveillance mechanism

- Deep immune profiling established a **direct mechanistic link between these novel T-cell clonotypes and intismeran-encoded neoantigens** (*Sullivan, R et al; poster #9564*)

- Study limitations include the small sample size of this phase 2 study, immature overall survival results, and translational findings requiring validation in larger cohorts. **The phase 3 INTerpath-001 study (NCT05933577) of adjuvant melanoma is fully enrolled**; additional studies are ongoing across tumor types

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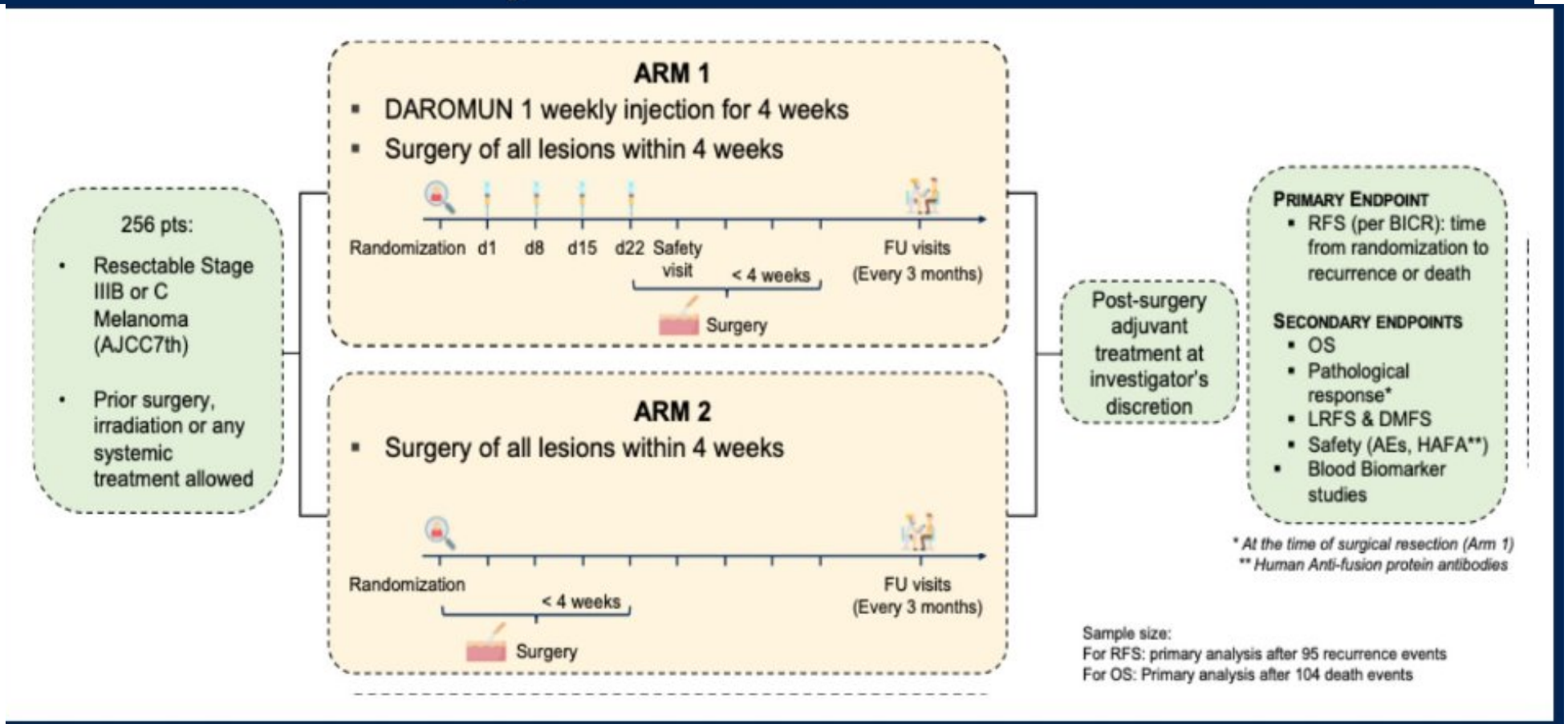
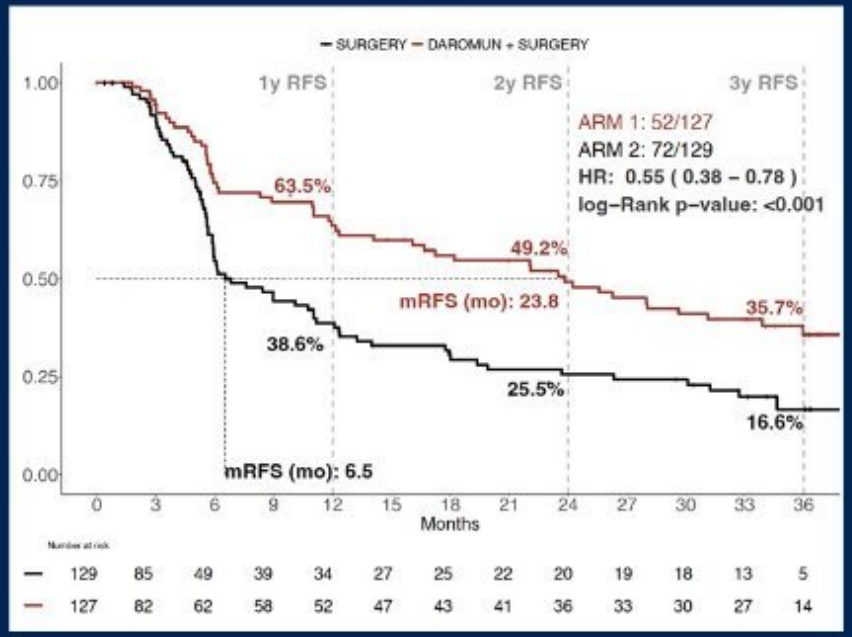
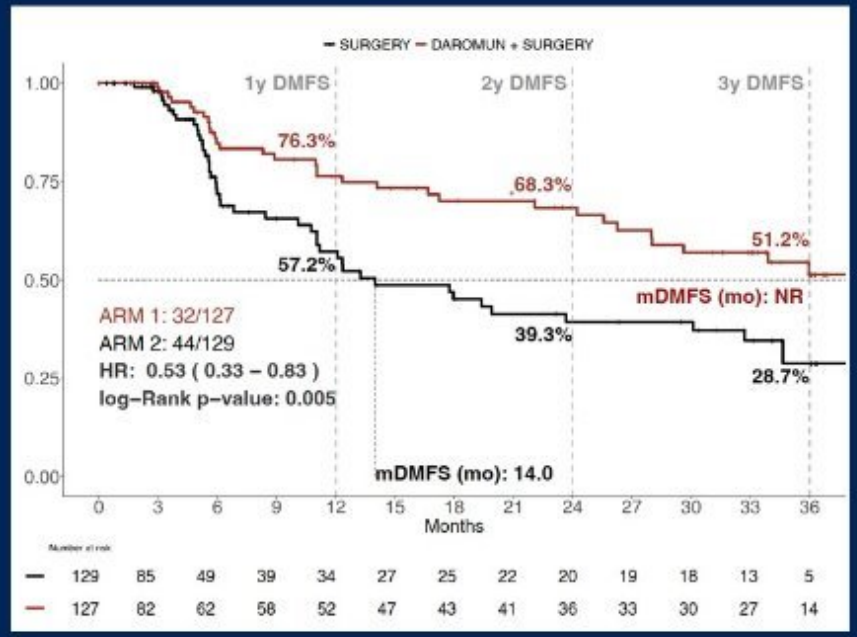
Neoadjuvant intralesional daromun (L19IL2/L19TNF) in resectable locally advanced melanoma: an update on the primary outcome and sensitivity analyses (EFS) from the PIVOTAL phase 3 trial.



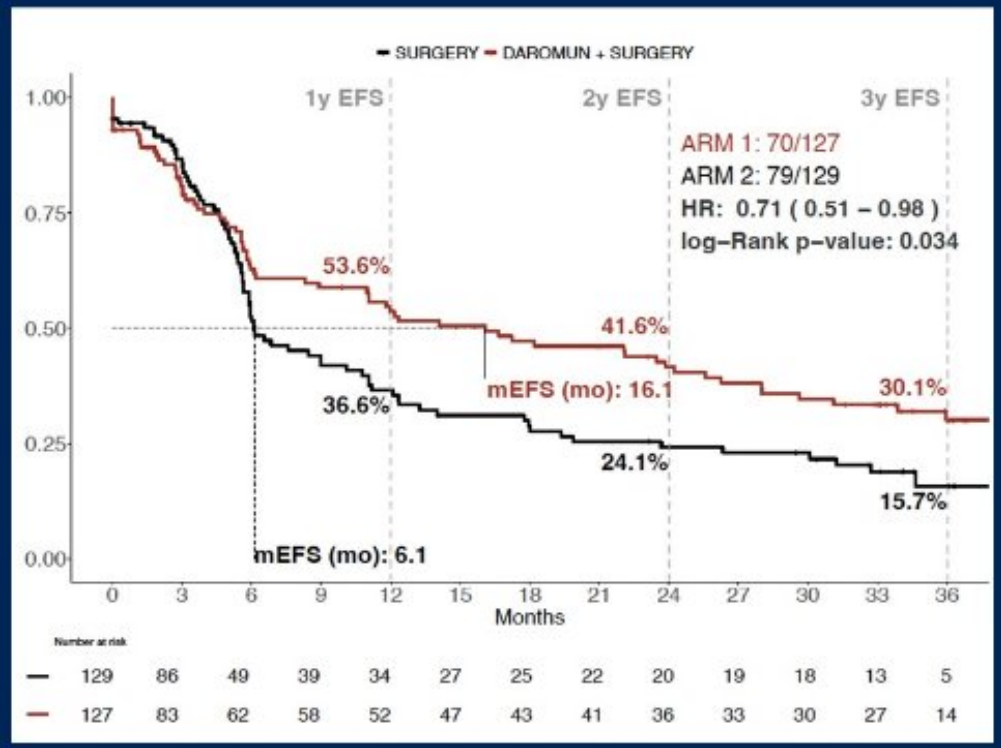
Results: updated KM curves for RFS and DMFS





The updated analysis confirms the clinically and statistically significant improvements for daromun in RFS and DMFS

Results: post-hoc analysis of event-free survival (EFS)



EFS is defined as time from randomization to disease progression (including unresectable disease at restaging) and treatment-related toxicity that precludes surgery, R2 resection, disease recurrence after surgery, or death from any cause

EFS analysis in the overall population is consistent with the RFS benefit for neoadjuvant daromun

Key Takeaway Conclusions

1

Daromun provides clinically significant RFS and DMFS benefits to stage III patients, including those who failed adjuvant systemic therapy. EFS analysis reinforces these findings

2

Intralesional daromun represents an effective, safe alternative for patients who failed or were not eligible to (neo)adjuvant ICIs

3

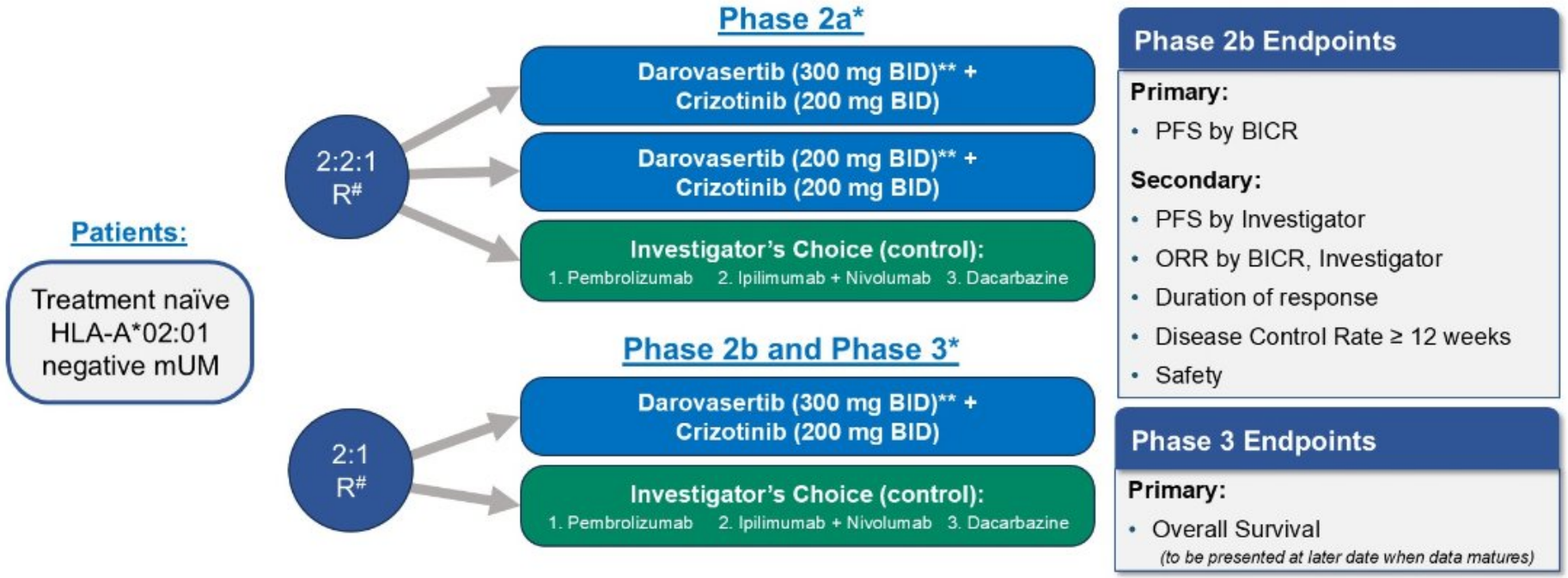
A confirmatory phase 3 neoadjuvant study in resectable stage III melanoma is ongoing in the US and various EU countries (NeoDREAM; NCT03567889)

2026 ASCO ANNUAL MEETING

Darovasertib Plus Crizotinib vs Investigator's Choice as First-Line Treatment for Patients with HLA-A2 Negative Metastatic Uveal Melanoma: Primary Results from the OptimUM-02 Trial

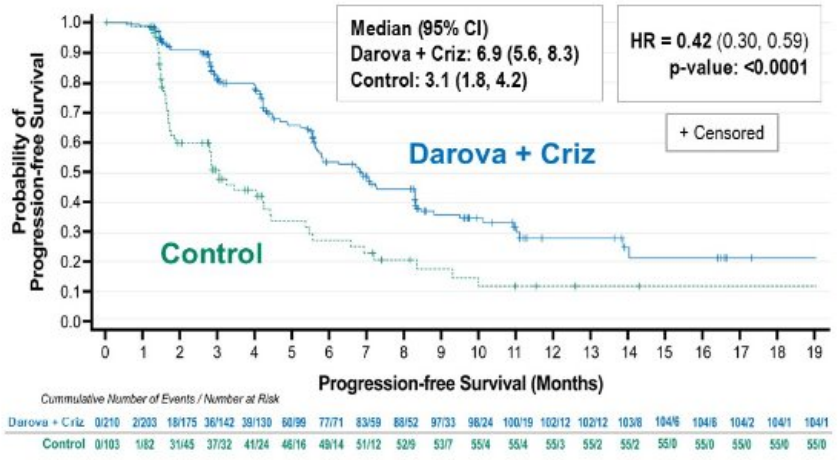
- 313 pacientes
- 80% Ipo-nivo rama control

Phase 2/3, multi-center, multi-arm, multi-stage, open-label study



Primary Efficacy Endpoint Results

BICR Assessment

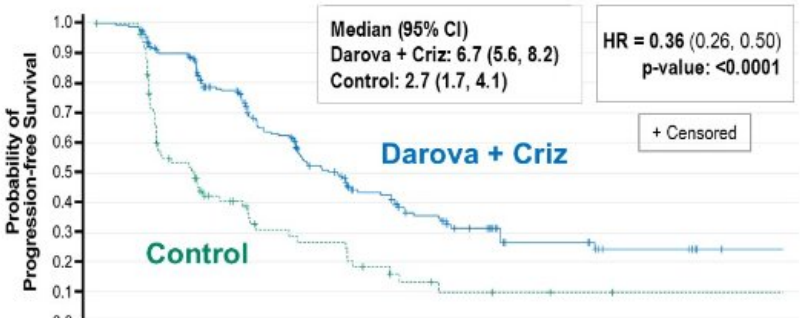


- Clinically meaningful and statistically significant i
- Reduction in the risk of progression or death:
  - 58% by BICR (HR: 0.42); 64% by investigat

Median follow-up for the population was 7.4 months. Median duration of treatment for darovasertib and crizotinib w
2.56, and 2.79 months, respectively.
BICR, blinded independent central reader. Darova + criz, darovasertib + crizotinib. HR, hazard ratio. PFS, progres

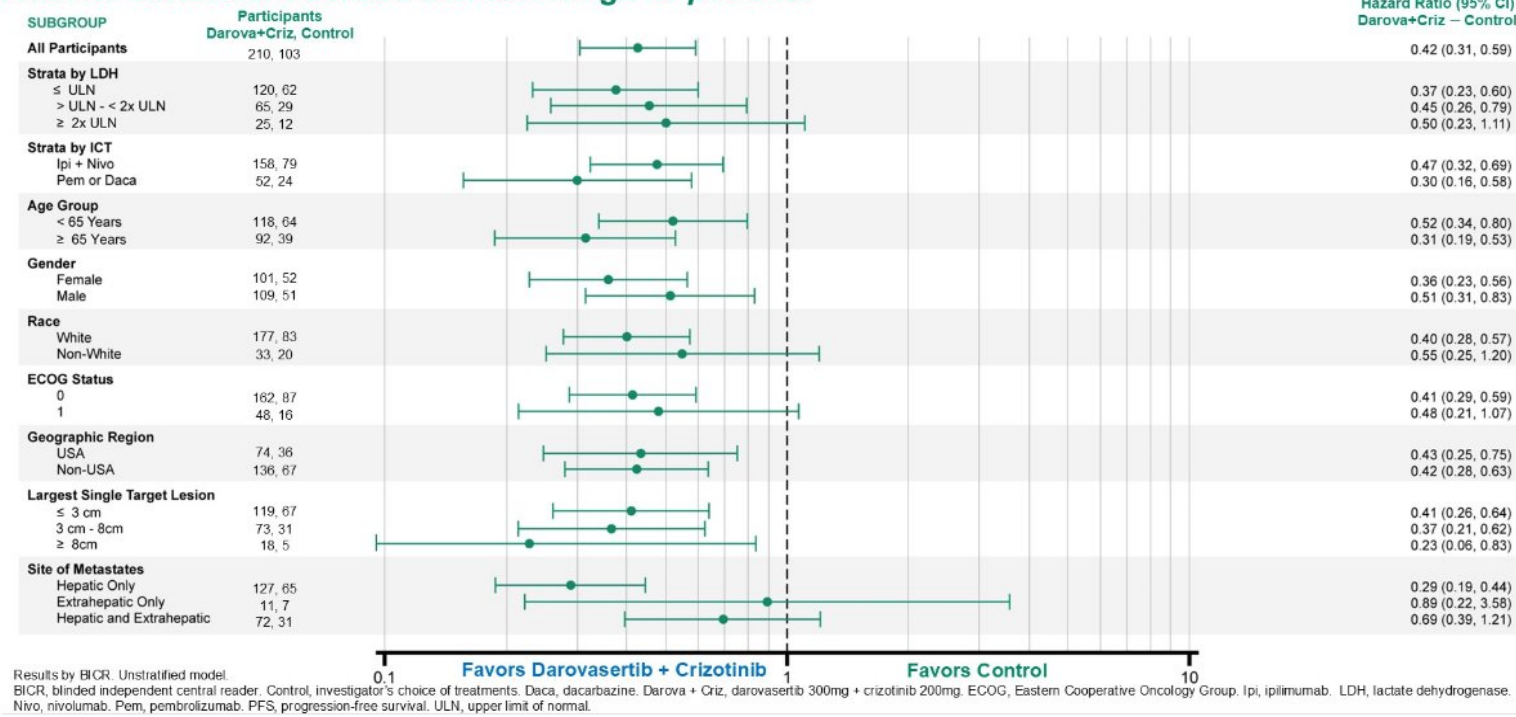
PRESENTED BY: Marlana Orloff, MD. Alexander & Johnston Family

Investigator Assessment



Primary Endpoint Results: PFS Subgroup Analysis

Results consistent across a broad range of patients



Results by BICR. Unstratified model.
BICR, blinded independent central reader. Control, investigator's choice of treatments. Daca, dacarbazine. Darova + Criz, darovasertib 300mg + crizotinib 200mg. ECOG, Eastern Cooperative Oncology Group. Ipi, ipilimumab. LDH, lactate dehydrogenase. Nivo, nivolumab. Pem, pembrolizumab. PFS, progression-free survival. ULN, upper limit of normal.

Summary

- In patients with HLA-A2-negative-mUM treated in the first-line setting, darovasertib +crizotinib demonstrated:
  - Clinically meaningful and significantly longer PFS vs investigator's choice (mPFS of 6.9 months vs 3.1 months, HR 0.42, indicating a 58% reduction in disease progression or death)
  - Significantly improved ORR (37.1% vs 5.8%) and DCR (73.3% vs. 31.1%) by BICR compared with the investigator's choice treatment, the majority (76.7%) were treated with ipilimumab + nivolumab
  - OS data is not yet mature; however, an early trend toward improved OS was observed with the darovasertib combination arm versus ICT. OS data will be presented at a future date
  - AEs consistent with prior safety profile, with low rate of TR-SAEs (9.2%) and discontinuations due to TRAEs for darovasertib and crizotinib (2.5 and 10% respectively)

The OptimUM-02 results support a potential new therapeutic standard for a disease with limited treatment options and poor prognosis

BICR, blinded independent central reader. IC, investigator's choice. DCR, disease control rate. HLA, human leukocyte antigen. HR, hazard ratio. mPFS, median progression free survival. mUM, metastatic uveal melanoma. ORR, objective response rate. TR-SAE, treatment-related serious adverse events. TRAE, treatment-related adverse events.

PRESENTED BY: Marlana Orloff, MD. Alexander & Johnston Family Endowed Clinical Director in Uveal Melanoma; Professor

2026 ASCO ANNUAL MEETING

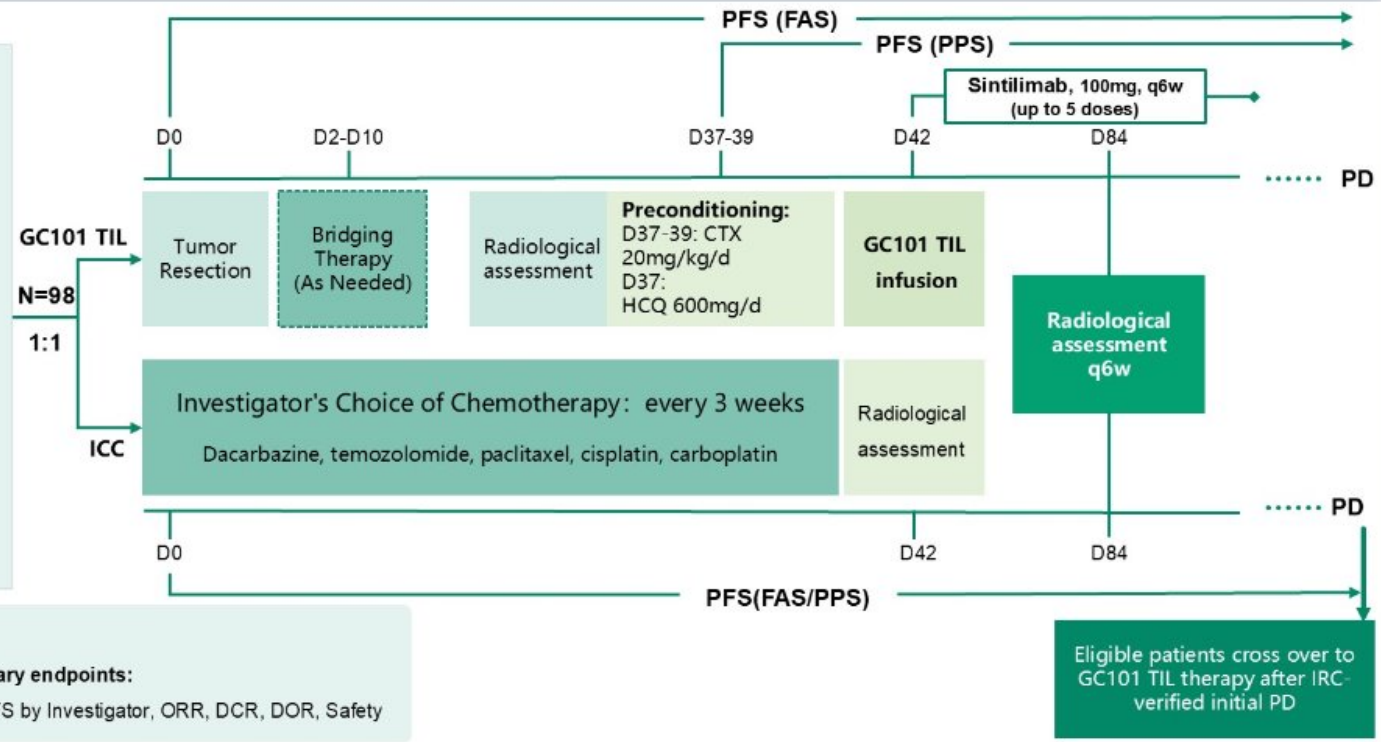
LBA9509

MIZAR-003 Trial:

A Multicenter, Randomized, Pivotal Phase II Trial of Autologous Tumor Infiltrating Lymphocytes (GC101 TIL) in Advanced Melanoma

Key Eligibility Criteria:

- Aged 18 to 70 years;
- Histologically confirmed unresectable or metastatic melanoma;
- Prior systemic therapy≥2 lines, anti-PD-1 failure;
- Feasible tumor tissue for resection (≥150mm^3) ;
- At least one remaining measurable target lesion.



Study Endpoints

Primary endpoint:
- PFS by IRC (RECIST v1.1)

Secondary endpoints:
- OS, PFS by Investigator, ORR, DCR, DOR, Safety

CTX, cyclophosphamide; DCR, disease control rate; DOR, duration of response; HCQ, hydroxychloroquine; ICC, Investigator's choice of chemotherapy; IRC, independent review committee; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; TIL, Tumor-Infiltrating Lymphocytes.

Baseline Characteristics

- A total of 99 pts were enrolled, over 70% were acral or mucosal melanomas.
- Baseline characteristics were similar between the two arms, but Lung and LN metas were more common in chemo
- As data cutoff, 35 pts received cell infusion (another 4pts not yet).
- The median infused cell dose was 42.90×10^9 (range, $4.62\text{-}53.92\times10^9$).

Characteristic	GC101 TIL (N=50)	ICC (N=49)	Total (N=99)
Age (years, median, range)	58 (29, 73)	59 (28,73)	58 (28,73)
Sex, n (Female, %)	28(56.0)	25(51.0)	53(53.5)
Melanoma subtype, n (%)			
Acral	**31(62.0)**	**26(53.1)**	**57(57.6)**
Cutaneous	**12(24.0)**	**12(24.5)**	**24(24.2)**
Mucosal	6(12.0)	9(18.4)	15(15.2)
Unknown primary	1(2.0)	2(4.1)	3(3.0)
Visceral metastasis, n (%)			
Lung	27(54.0)	32(65.3)	59(59.6)
Liver	9(18.0)	8(16.3)	17(17.2)
Lymph node	38(76.0)	41(83.7)	79(79.8)
Bone	9(18.0)	6(12.2)	15(15.2)

Characteristic	GC101 TIL (N=50)	ICC (N=49)	Total (N=99)
ECOG performance status, n (%)			
1	31(62.0)	37(75.5)	68(68.7)
0	19(38.0)	12(24.5)	31(31.3)
Gene mutation, n (%)			
BRAF mutated	5(10.0)	2(4.1)	7(7.1)
NRAS mutated,	6(12.0)	5(10.2)	11(11.1)
Target Lesions Sum of Diameter (mm, Mean ± SD)	61.8±32.5	75.0±39.7	68.4±36.7
Number of prior systemic therapy lines (n, median, range)	2(2,5)	2(2,5)	2(2,5)
Lactate dehydrogenase (LDH), n (%)			
≤ ULN	37(74.0)	36(73.5)	73(73.7)
> ULN	13(26.0)	13(26.5)	26(26.3)

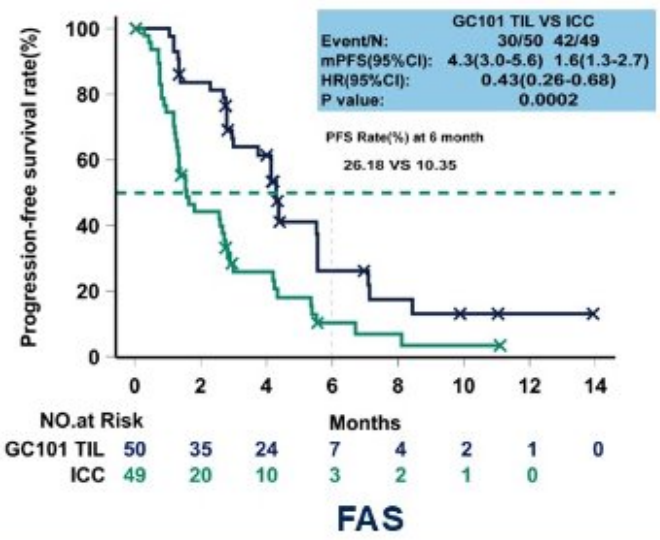
ECOG, eastern cooperative oncology group; ICC, investigator's choice of chemotherapy; LDH, lactate dehydrogenase; SD, standard deviation; TIL, tumor-infiltrating lymphocytes; ULN, upper limit of normal.

Data cutoff date: May 12, 2026.

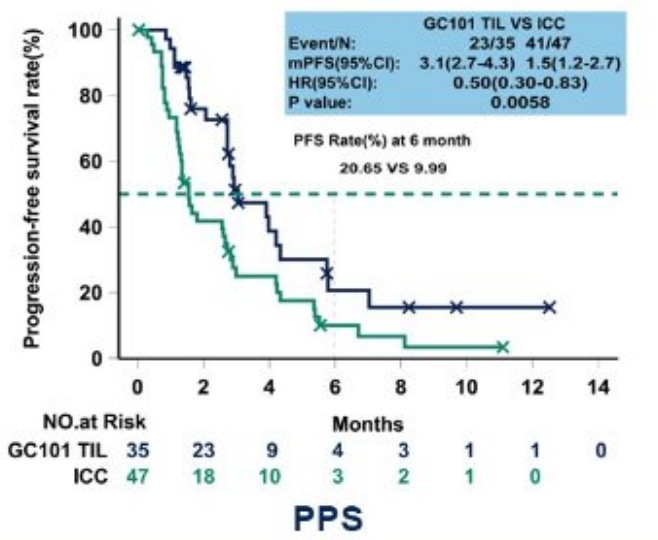
GC101 TIL Significantly Improved PFS *vs.* ICC

- **Primary endpoint met in FAS**
  - Median PFS: 4.3 *vs.* 1.6 months, HR = 0.43, p = 0.0002.
- Even with 57% chemo cross-over, a survival benefit trend showed in the TIL group.
- Longest DOR* already exceeding 12 months.

PFS

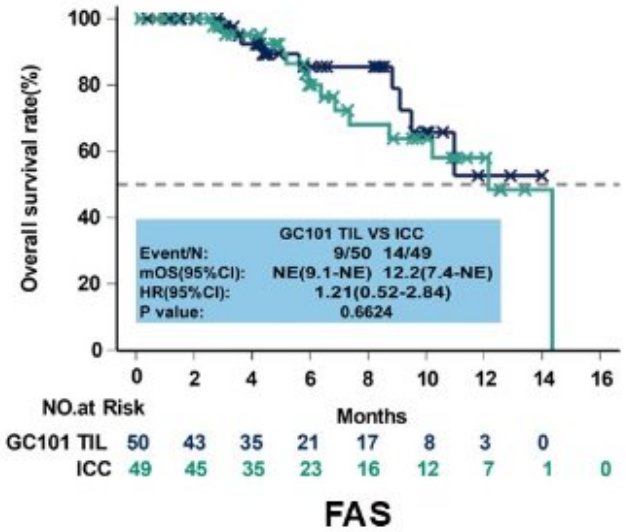


FAS



PPS

OS *



FAS

* not yet mature

CI, confidence interval; HR, hazard ratio ; ICC, investigator's choice of chemotherapy; OS, overall survival; PFS, progression-free survival; TIL, tumor-infiltrating lymphocytes.

Data cutoff date: May 12, 2026.

Overall Safety Profile

- GC101 TIL group had a higher overall incidence of any AEs and TRAEs (both any grade or ≥3).
- Grade ≥3 TRAEs were primarily lymphodepletion-related hematologic toxicities.

TEAEs in ≥30% of Patients, n (%)	GC101 TIL (N=50)	ICC (N=49)
Any adverse event	47 (94.0)	45 (93.8)
Leukopenia	40 (80.0)	22 (45.8)
Neutropenia	39 (78.0)	18 (37.5)
Anemia	32 (64.0)	20 (41.7)
Lymphopenia	34 (68.0)	15 (31.3)
Pyrexia	31 (62.0)	1 (2.1)
Thrombocytopenia	24 (48.0)	15 (31.3)
Nausea	19 (38.0)	18 (37.5)
Rash	18 (36.0)	2 (4.2)
Constipation	16 (32.0)	12 (25.0)
Hypokalemia	15 (30.0)	8 (16.7)

Common Grade ≥3 TRAEs (incidence ≥5%) , n (%)	GC101 TIL (N=50)	ICC (N=49)
Any TRAE ≥3	34(68.0)	13(27.1)
Neutropenia	32(64.0)	10(20.8)
Leukopenia	32(64.0)	7(14.6)
Lymphopenia	24(48.0)	3(6.3)
Anemia	7(14.0)	2(4.2)
Thrombocytopenia	5(10.0)	2(4.2)

AE, adverse event ; ICC, Investigator's choice of chemotherapy; TEAE, treatment-emergent adverse event; TIL, tumor-infiltrating lymphocytes; TRAE, treatment-related adverse event.

Data cutoff date: May 12, 2026.

Conclusions

- **This is the first RCT of TIL in late-line anti-PD-1 refractory advanced melanoma**
  - mPFS: 4.3 *vs.* 1.6 months (HR 0.43, p = 0.0002) (**Primary endpoint met**);
  - ORR: 42.0% *vs.* 6.1%; DCR: 72.0% *vs.* 42.9%;
  - OS and DoR were not yet mature.

- **Favorable safety profile**
  - Low-intensity preconditioning (CTX + HCQ) and no IL-2 infusion;
  - No IL-2-related toxicities (capillary leak syndrome, hypotension, febrile neutropenia);
  - No need for ICU admission, shorter hospitalization and rapid recovery.

- **Clinical implication**
  - GC101 TIL represents an effective, less toxic, and more accessible treatment option for anti-PD-1 refractory advanced melanoma.

Data cutoff date: May 12, 2026.

2026 ASCO ANNUAL MEETING

Abstract #: 9507

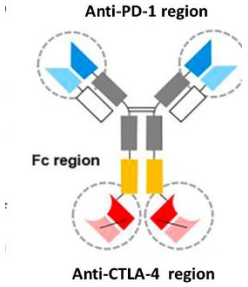
Oral Abstract Session

OBX-115 engineered tumor-infiltrating lymphocyte (TIL) cell therapy with regulatable membrane-bound IL15 (mbIL15) in patients with advanced melanoma that has progressed on/after immune checkpoint inhibitors (ICI): Phase 2 results.

- Fase 1-2 melanoma metastásico refractario a IO
- Terapia celular TILs modificados
- Expresión aumentada y modulada de IL-15
- TR 67%, incluye RC.

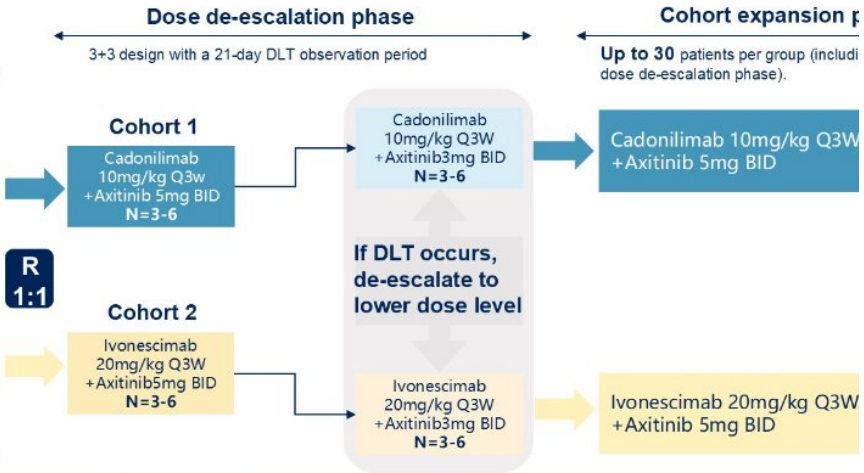
2026 ASCO ANNUAL MEETING

Cadonilimab or Ivonescimab Plus Axitinib in Metastatic Mucosal Melanoma: Results from a Phase Ib Trial



- A single-center, open-label Phase Ib clinical study (NCT06424626)

Key Eligibility Criteria:
- Aged 18 to 70 years.
- Histologically confirmed metastatic mucosal melanoma.
- No prior systemic therapy (neoadjuvant or adjuvant therapy were allowed with disease progression more than 6 months after treatment completion).
- At least one measurable tumor lesion per RECIST 1.1 criteria.
- ECOG PS.0 or 1



Primary Endpoints:
Safety assessment: Dose-limiting toxicity (DLT), incidence and severity of adverse events, and maximum tolerated dose (MTD) of axitinib.

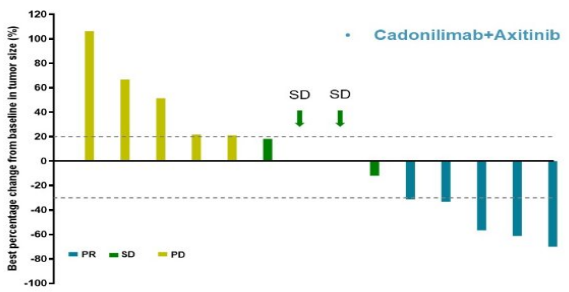
Secondary Endpoints:
Efficacy assessment: **Objective Response Rate (ORR)**, Disease Control Rate (DCR), **Progression-Free Survival (PFS)** and Overall Survival (OS), assessed per RECIST Ve

ORR

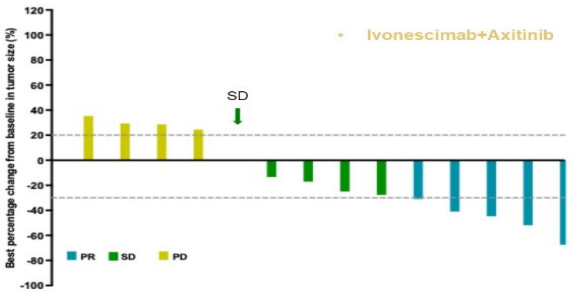
- A total of 28 patients were evaluable for efficacy assessment.

	Cadonilimab+Axitinib（n=14） n (%)	Ivonescimab+Axitinib（n=14） n (%)
PR	5 (35.7%)	5 (35.7%)
SD	4 (28.6%)	5 (35.7%)
PD	5 (35.7%)	4 (28.6%)
ORR	35.7%	35.7%
95% CI	14.9% ~ 61.5%	14.9% ~ 61.5%
DCR	64.3%	71.4%
95% CI	38.68%～83.74%	45.35%～88.28%

Waterfall Plot



Tumor shrinkage occurred in 6/14 patients (42.9%).



Tumor shrinkage occurred in 9/14 patients (64.3%).

CONCLUSIONES

- Vacunas individualizadas RNAm
  - **Vacuna de ARNm + pembrolizumab redujo el riesgo de recurrencia un 49%**
  - El riesgo de **metástasis a distancia disminuyó un 59 %**
- **Neoadyuvancia: Actualización Daromun intralesional**
  - Precisa fase 3
  - ¿Cómo lo encajamos con IO neo/adyuvante?
- **Darovasertib + Crizotinib en 1ª linea mm uveal HLA-A2 negativo**
- TILs modificados varios en fase II.

¡Gracias!

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