

7. ulusal CERRAHİ ONKOLOJİ KONGRESİ
12-15 AĞUSTOS 2024, 1. BUĞSİ LUXURY RESORT HOTEL

MALİGN MELANOMDA ONKOLOJİK YÖNETİM
DOÇ. DR. TOLGA KÖŞECİ
ÇUKUROVA ÜNİVERSİTESİ-TİBBİ ONKOLOJİ BD
15.12.2024

Sunum planı

- Giriş
- Biyoloji
- Melanomun sınıflandırması
- Evre
- Adjuvan ve Neoadjuvan tedavi
- Metastatik hastalık tedavisi

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Eras in the cancer treatment

Ann Surg. 1894; 20: 497-555

AC Surgery and Radiation 1950 Chemotherapy 2001 Targeted therapy 2011 IO

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IMMUN KONTROL NOKTA İNHİBİTÖRLERİ ETKİ MEKANİZMASI

Drake, C. G. et al. Nat. Rev. Clin. Oncol 2013

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MALİGN MELANOM TİPLERİ

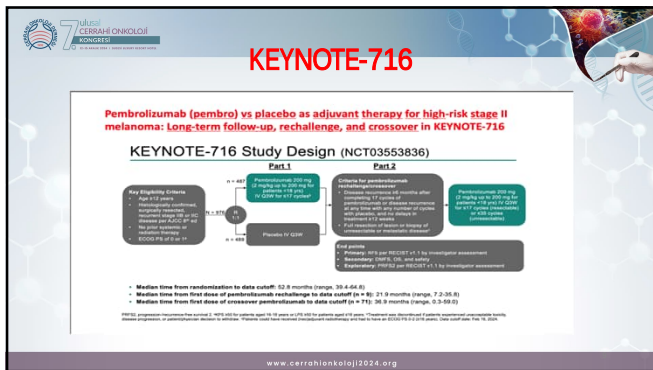
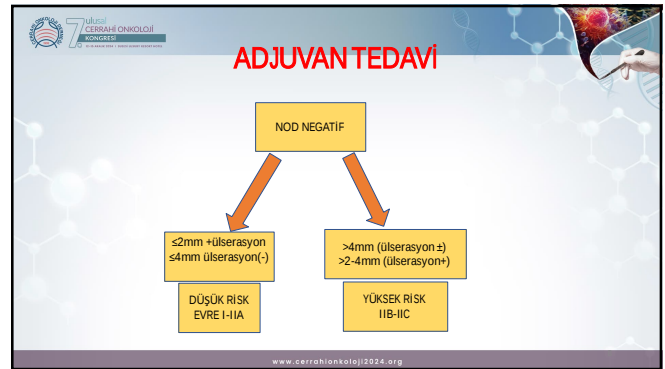
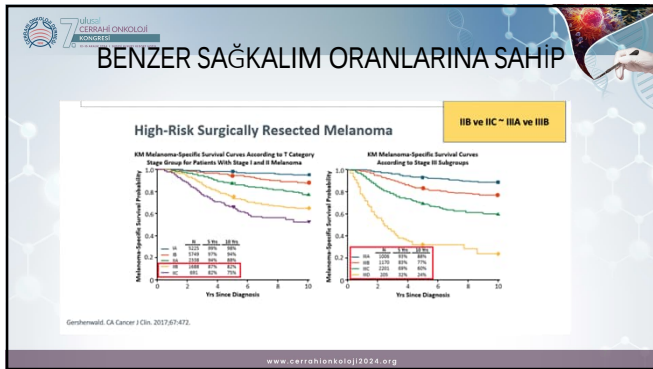
		Mucosal	Acral	Cutaneous
Incidence (% all stages)	Asian	20-25%	40%	35%
	Caucasian	<5%	<5%	95%
UV-signature		-	-	+
Tumor mutational burden		↓	↓	↑
Driving mutation	BRAF	5%	10-30%	40-50%
	NRAS	15%	10-20%	30%
	c-KIT	5%	5-10%	<5%

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EVRELEME

Stages of Melanoma

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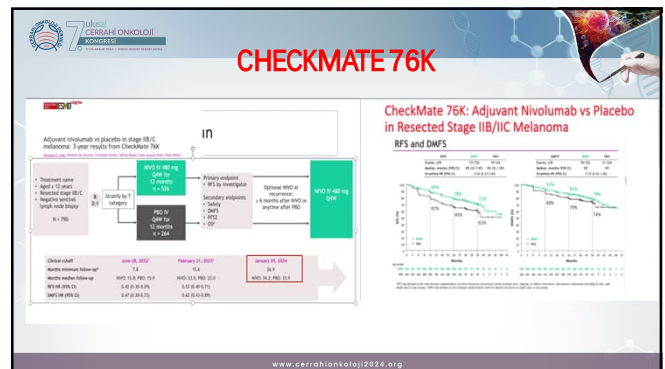
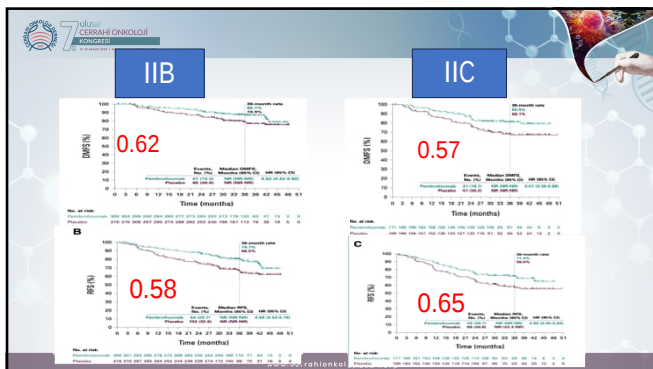
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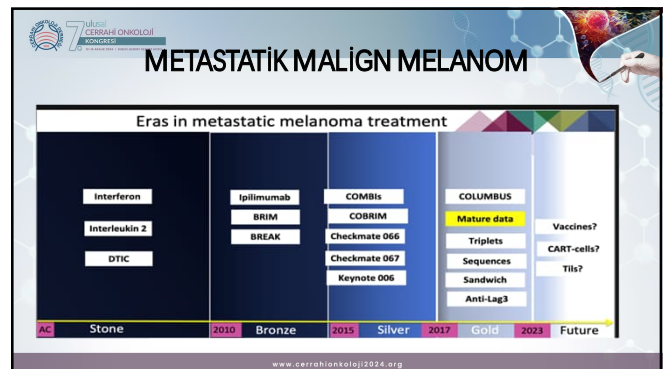
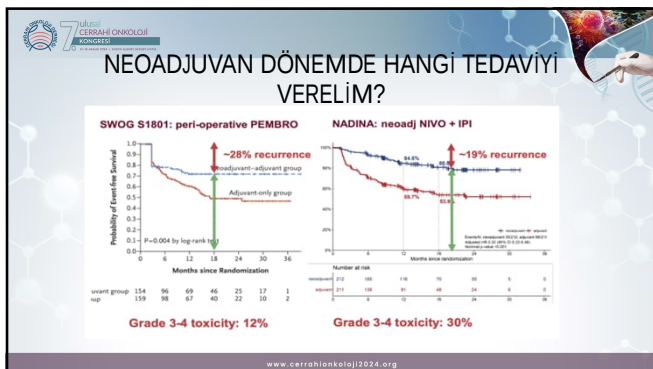
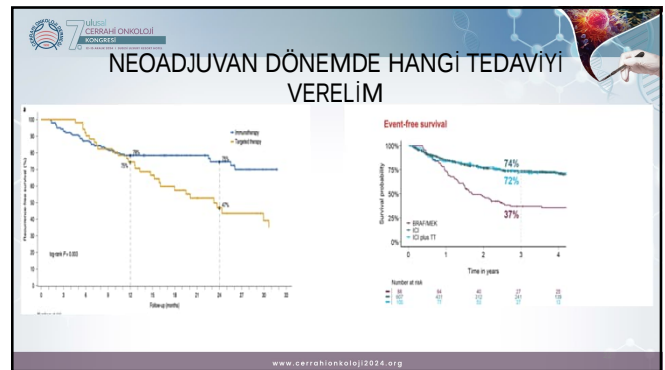
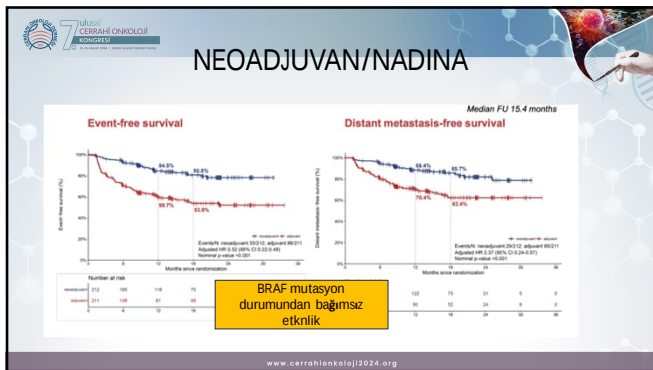
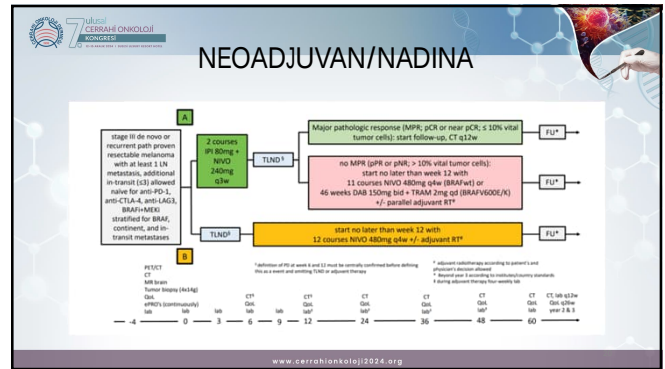
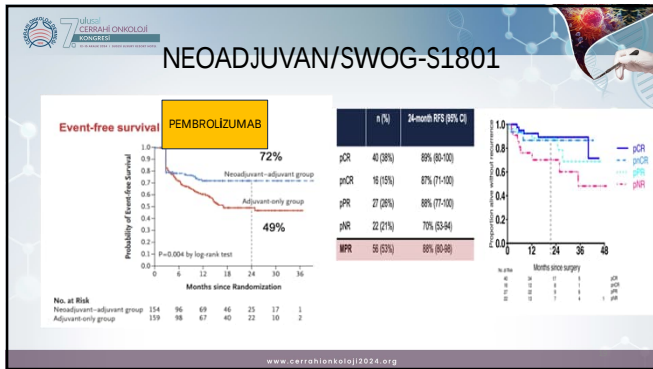
T3	>2.0-4.0 mm	Unknown or unspecified
T3a	>2.0-4.0 mm	Without ulceration
T3b	>2.0-4.0 mm	With ulceration
T4	>4.0 mm	Unknown or unspecified
T4a	>4.0 mm	Without ulceration
T4b	>4.0 mm	With ulceration

Stage IIB	T3b	NO	MO
	T4a	NO	MO
Stage IIC	T4b	NO	MO

%98

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7. ULUSAL CERRAHE ONKOLOJİ KONGRESİ

METASTATİK HASTALIKTA/BRAF+MEK İNHİBİTÖRLERİ

Studies	Phase	N	Arms	EP 1	mOS	mPFS	RR (C)
COMBI-v	III	694	Dabrafenib+Trametinib vs Vemurafenib	OS	25.6	12.6	66 % (19)
COMBI-d	III	340	Dabrafenib+Trametinib vs Dabrafenib	PFS	25.1	11.0	68 % (19)
co-BRIM	III	500	Vemurafenib+Cobimetinib vs Vemurafenib	PFS	22.3	12.2	69 % (21)
COLUMBUS	III	577	Encorafenib+Bimimetinib vs Vemurafenib	PFS	33.6	14.9	63 %

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7. ULUSAL CERRAHE ONKOLOJİ KONGRESİ

METASTATİK HASTALIK YÖNETİMİ



Singles
Nivolumab
Pembrolizumab
Ipilimumab

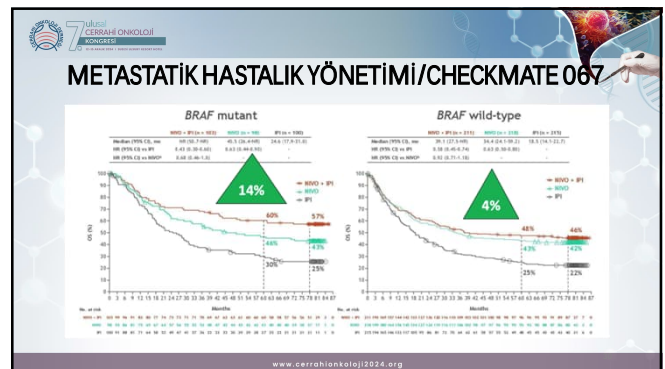
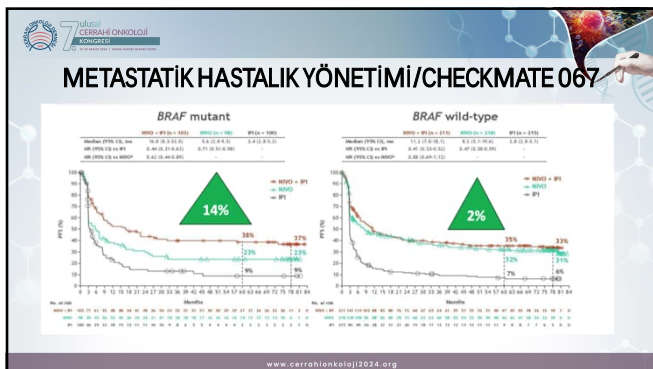
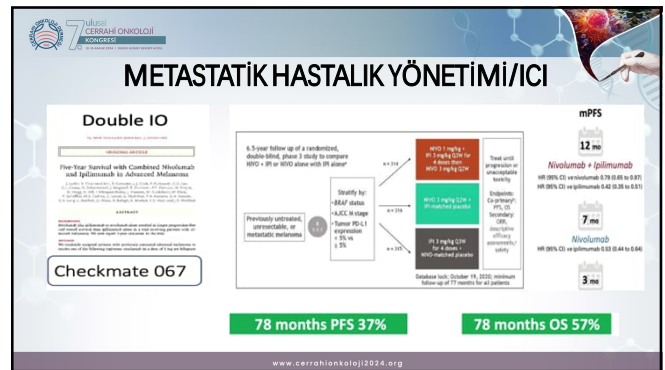
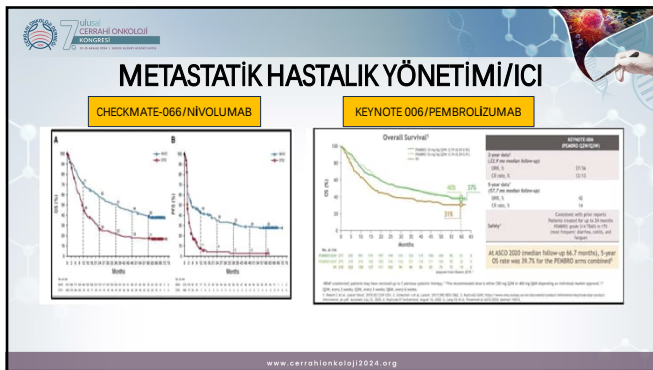


Doubles
D+T
V+C
E+B
Ipi+Nivo
Nivo+Relatimab



Triplets
Atez+ V+C

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CERRAHİ KOZMOLOJİ
KONGRESİ



HANGİ TEDAVİ İLE BAŞLAYALIM

Sequence Phase 2r: SECOMBIT



Trial Design

- Non-comparative, randomized, controlled
- Phase II study
- AKA, A, B, C

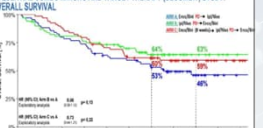
Patient Population

- Previously untreated metastatic melanoma
- AKA: 100% untreated
- n=22, 272, 229

Outcomes

- AKA: 100% death
- Group B: 4 patients were not counted in Arm B
- Specific finding in treatment discontinuation after using anti-

SEQUENTIAL COMBO IMMUNO AND TARGET THERAPY (SECOMBIT) STUDY: OVERALL SURVIVAL



Time (months)	SECOMBIT (n=100)	SECOMBIT + A (n=100)	SECOMBIT + B (n=100)
0	100	100	100
12	85	80	75
24	75	65	60
36	65	55	50
48	55	45	40
60	45	35	30
72	35	25	20
84	25	15	10
96	15	10	5
108	10	5	0

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HANGI TEDAVİ İLE BAŞLAYALIM

CERHAHONKOLOJİ
 GASTROENTEROLOJİ
 KOLONREKTAL

Sequence Phase 3: Dreamseq

2024 mutant landscape → **Imagize** → **Single IO** → **TT** → **Single IO**

Step 1: Arm A* (Synthetic + metabolic inhibition followed by immunotherapy maintenance) → Arm C (Synthetic + metabolic inhibition) → Arm C* (Synthetic + metabolic inhibition followed by immunotherapy maintenance) → Arm D* (Synthetic + metabolic inhibition followed by immunotherapy maintenance)

Step 2: Single IO → TT → Single IO

DREAMSEQ Overall Survival: Step 1 + Step 2

Overall Survival: Step 1 + Step 2

Time (months)	Control (n=10)	Treatment (n=10)
0	10	10
12	8	8
24	6	6
36	4	4
48	3	3
60	2	2
72	1	1
84	1	1
96	1	1
108	1	1
120	1	1

Overall Survival: Step 1 + Step 2

Optimal Response Rate

Time (months)	Control (n=10)	Treatment (n=10)
0	10	10
12	8	8
24	6	6
36	4	4
48	3	3
60	2	2
72	1	1
84	1	1
96	1	1
108	1	1
120	1	1

Optimal Response Rate

* Combination treatment and Treatment arms are not mutually exclusive.

† Data for the combination treatment arms is not available for Patients With Advanced Stage Disease. See Results.

‡ Data for the combination treatment arms is not available for Patients With Advanced Stage Disease. See Results.

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SONUÇ

Treatment Regimen	Comparison	Outcome
Standard of care pre-2010	Surgery vs Observation	Med RFS 25.6 mo 5-yr RFS ~35%
2010 EORTC 18071	Surgery vs Adjuvant IFN-α	HR 0.62 vs obsn (DFS)
2017-18 KEYNOTE 054 CheckMate 238	Surgery vs Adjuvant CTLA-4	HR 0.75 vs obsn (RFS) 5-yr RFS ~41%
2022 SWOG S1801	Neoadjuvant PD-1 vs Surgery vs Adjuvant PD-1	HR 0.57 vs surgery alone (RFS) HR 0.65 vs CTLA-4 (RFS) 5-yr RFS ~55%
2024 NADINA	Neoadjuvant PD-1 plus CTLA-4 vs Surgery vs Response-directed adjuvant PD-1 or BRAF/MEX	HR 0.32 vs adjuvant PD-1 (EFS)



13. CERRAHİYA ONKOLOJİ KONGRESİ

SONUÇ



Medical options

Non-mutant BRAF melanoma (4 options)



Singles

Nivo
Pembro



Doubles

Ipi+Nivo
Nivo+Relatimab

MANAGEMENT OF METASTATIC MELANOMA

Medical options

Mutant BRAF melanoma (7 options)

First line



Singles

Nivo
Pembro
Ipi



Doubles

D+I
V+V
E+E
Ipi+Nivo
Nivo+Relatimab



Triples

Atez+V+V

Melanoma, 2023

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TEŞEKKÜRLER....

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