Novinky v léčbě karcinomu močového měchýře z pohledu onkologa

Poprach A, Lakomý R

MOU a LF MU

09/2020

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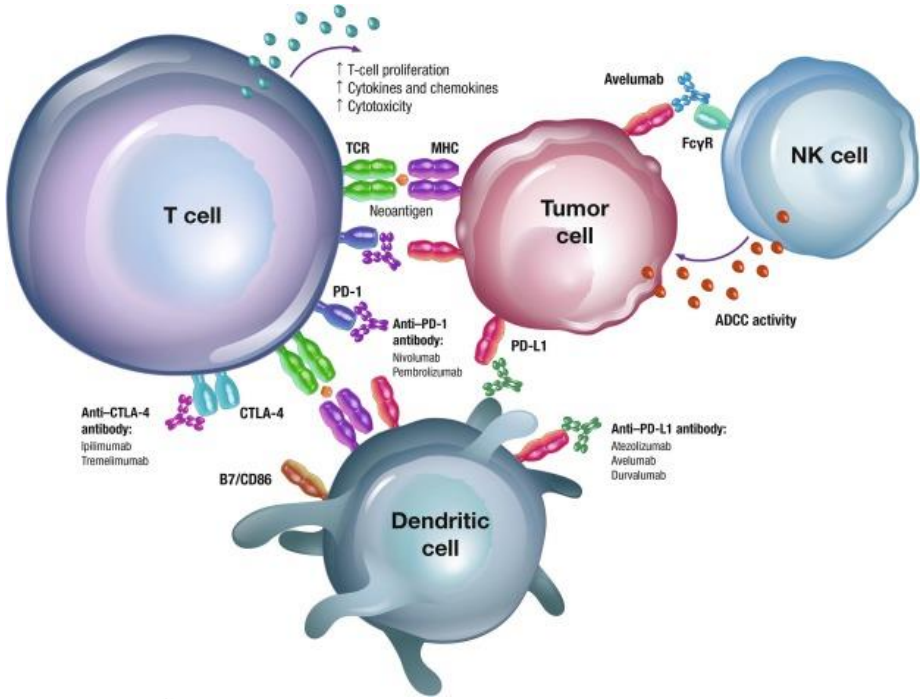
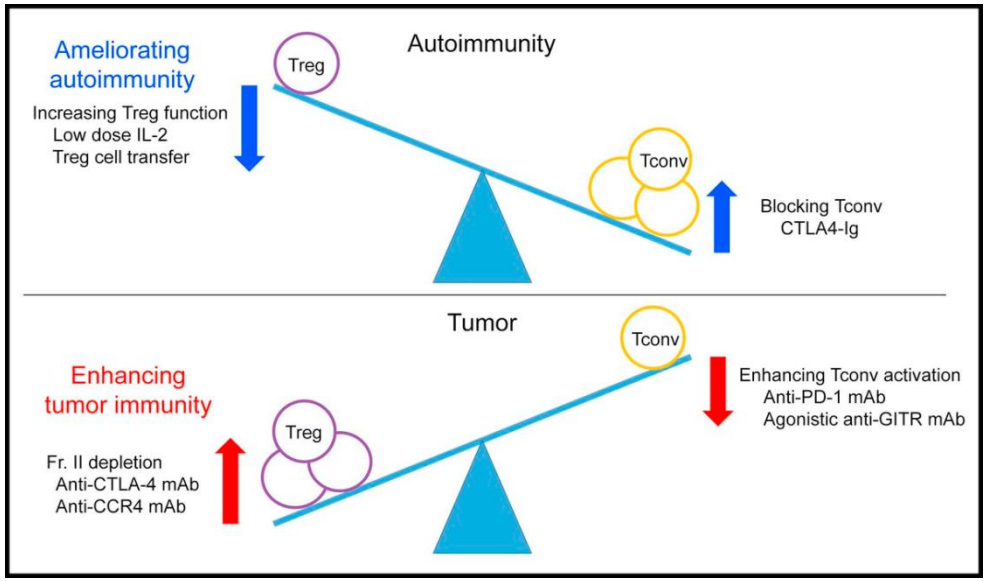
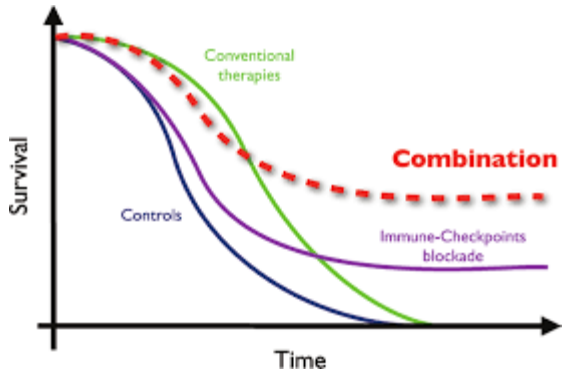
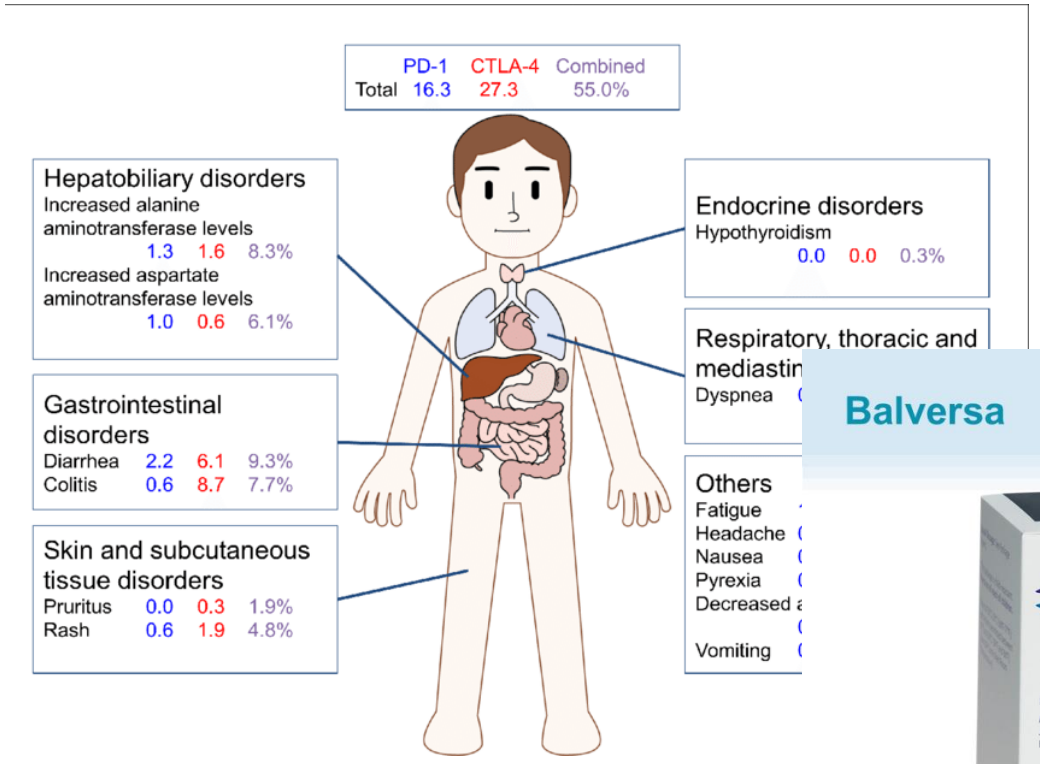
Chemoterapie…stále základ naší léčby…ale imunoterapie bude budoucností





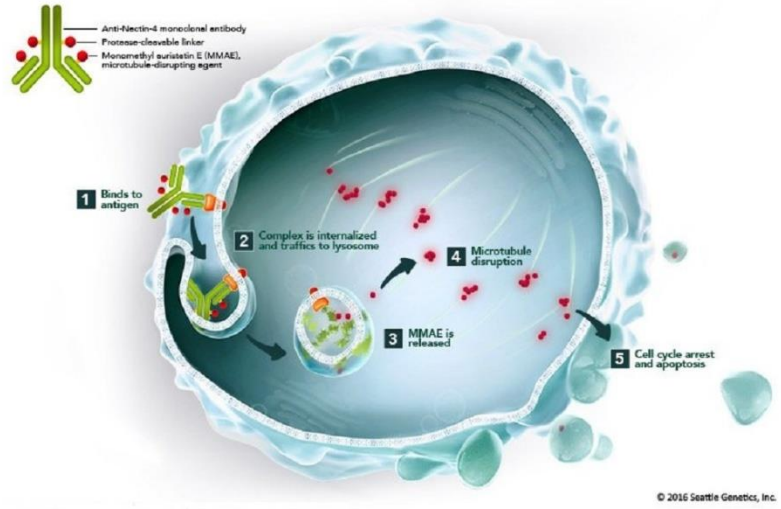


Imunoterapie však přináší i rizika:



Vývoj však nepřináší jen imunoterapii

Enfortumab vedotin



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T2-T4a a N1 (2,3) onemocnění

- (T1, Tis: při selhání BCG v USA… imunoterapie pembrolizumab…“ with BCG-unresponsive, high-risk, non-muscle invasive bladder cancer with Tis with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy“)
- Zpět k T2 onemocnění- základem onkologické léčby je neoadjuvance na bázi **CISPLATINY**!!!
- Preference DDP/Gem- 4x á 21 dní, nebo studie či DD M-VAC
- Cíl: downstaging tumoru a eradikace mikrometastáz
- **A poté RACE, nebo CHT/RT**

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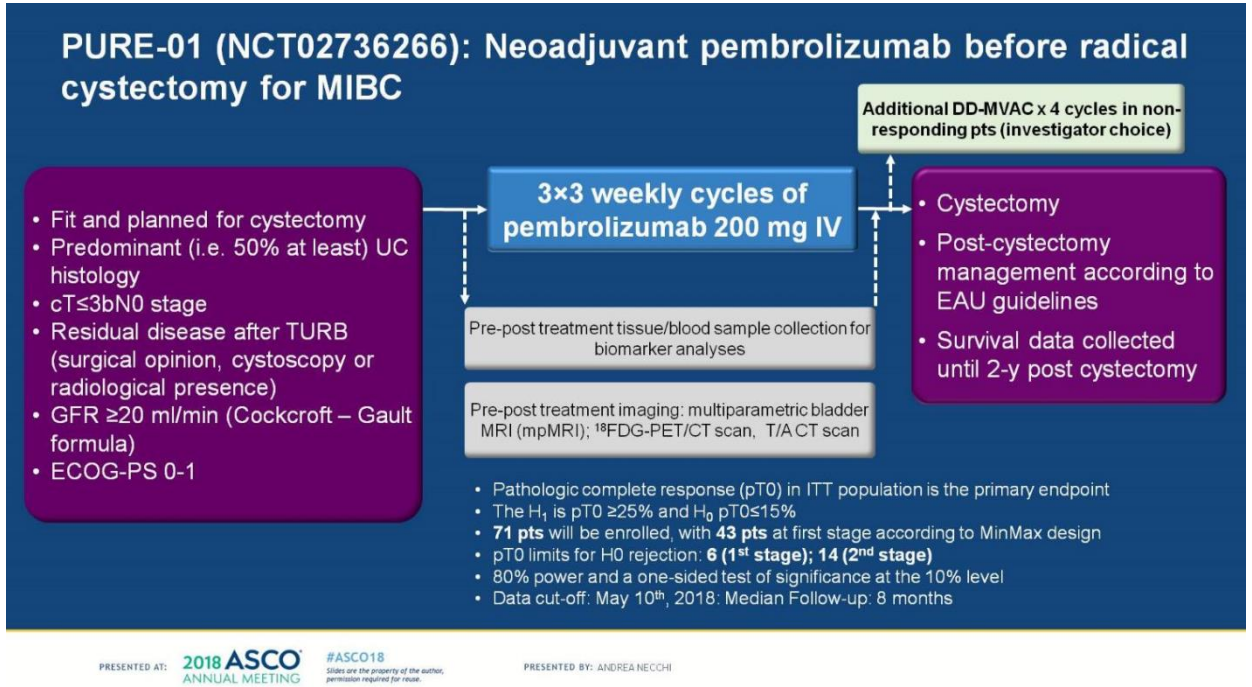
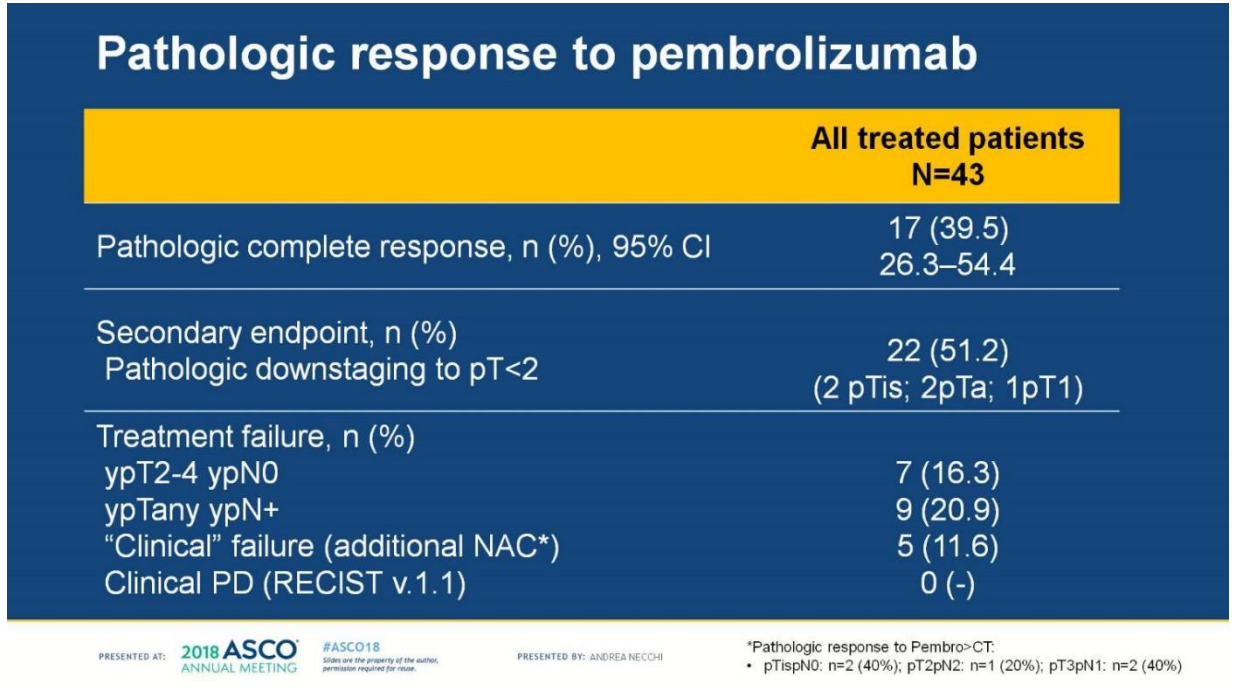
Cisplatina „unfit“ vs. „fit“

ECOG PS ≥ 2
Clearence kreatininu <60ml/min
Neuropatie stupně ≥ 2
Srdeční selhání stupně III a více
Audiometrická ztráta sluchu stupně ≥ 2

T2-T4a a N1 (2,3) onemocnění - budoucnost

- PURE-01 studie II.fáze

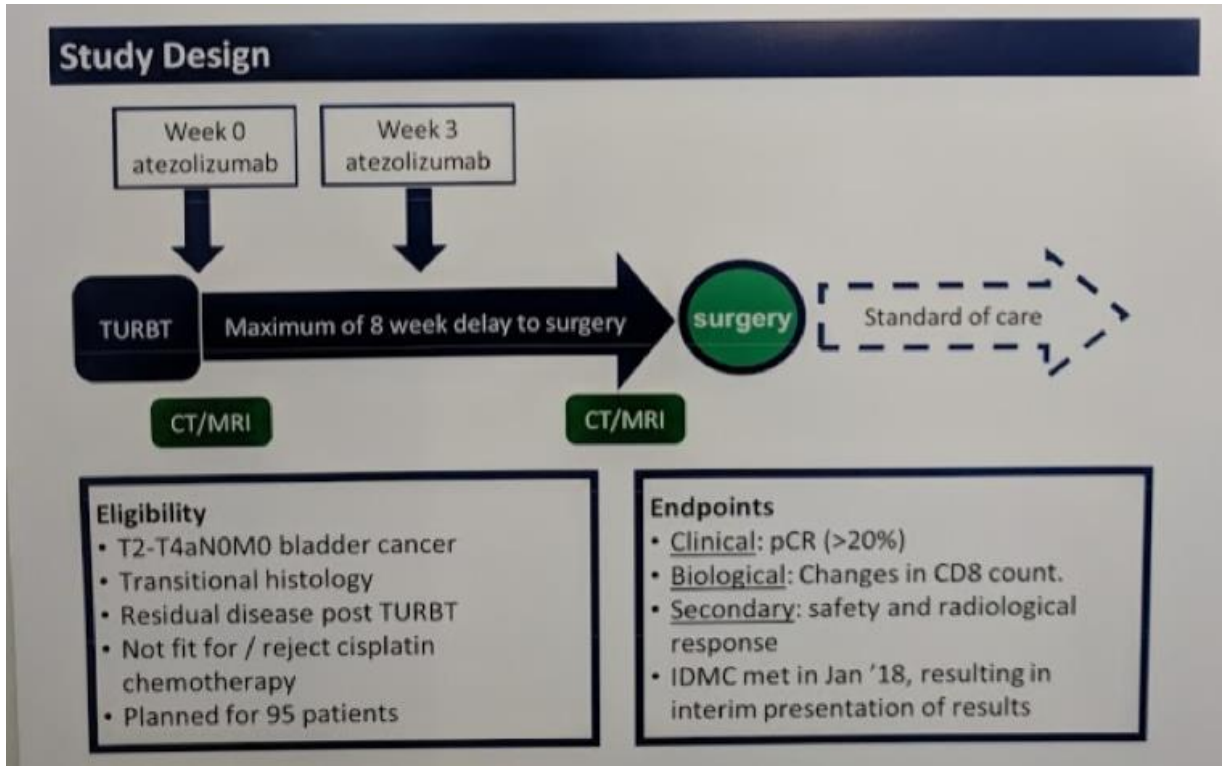




Presented By Andrea Necchi at 2018 ASCO Annual Meeting

T2-T4a a N1 (2,3) onemocnění - budoucnost

- Studie ABACUS- II.fáze



Powles T, et al. ASCO 2018. Abstract 4506

T2-T4a a N1 (2,3) onemocnění - budoucnost

Characteristic	Pembrolizumab (n = 43)[1]	Atezolizumab (n = 68)[2]
Eligibility criteria	T2-T3b; N1 allowed	T2-T4a; N0 only
Cisplatin eligible, %	100	0
Received neoadjuvant CT, %	12	0
Duration of neoadjuvant checkpoint inhibition	3 cycles (9 wks)	2 cycles (6 wks)
Safe	Yes	Yes
Pathological CR (pT0), %	40	29
Available biomarker data	Yes	Yes

pT0 Rates With CT:

Gem/Cis, 15% to 32%

DD MVAC, 26% to 43%

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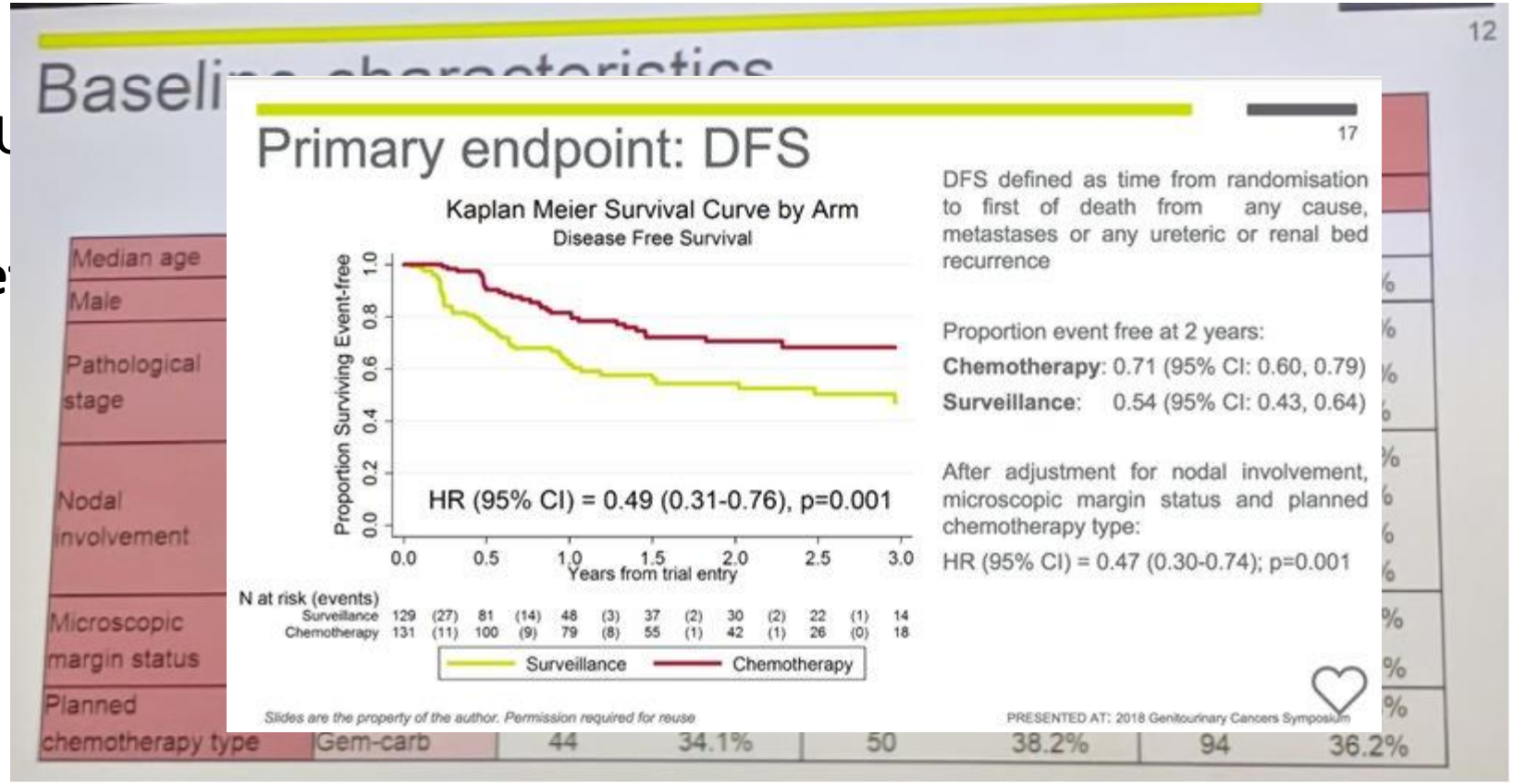
1. Necchi A, et al. ASCO 2018. Abstract 4507. 2. Powles T, et al. ASCO 2018. Abstract 4506.

Co po RACE?

- Adjuvance…pT3-pT4, N+ a asi u lymfovaskulární invaze, pokud **nebyla podána** neoadjuvance (CISPLATINA)
- Studie **POUT**!!!:
  - Studie III. fáze UTU
    vs. sledování.
  - **DFS HR 0,47!; 2 le**



Jones et al., ESMO 2019

Co po RACE?

- Novinka…zase imunoterapie…studie NIAGARA…durvalumab
  - Perioperační DDP/GEM+ durvalumab+ RACE+ následně durvalumab
- NABUCCO nivolumab a ipilimumab perioperační
- Atd…

Metastatické postižení

- Nutné rozlišení cisplatina „unfit“ vs. „fit“ pacienti; a nově „unfit platina pacienti „
- Stanovení míry exprese PD-L1- bohužel různé metody

- **V první linii paliativní léčby:**
  - Pro pacienty **cisplatina fit**: **cisplatina+ gem**
  - **Cisplatina unfit**: **imunoterapie při positivitě PD-L1 (pembro nebo atezolizumab)**, …bohužel v ČR karboplatina/ gem
  - **Platina unfit**: USA imunoterapie…v ČR…BSC?, monoterapie

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První linie paliativní léčby mUC: **cisplatina fit**

	Sternberg 1989[1]	Von Der Maase 2000, Roberts 2006[2,3]	Sternberg 2006[4]	Dreicer 2004[5]	Kaufman 2000[6]	EORTC 30987[7]
Therapies	M-VAC*	GC*[8] vs M-VAC	DD-M-VAC*† vs M-VAC*	carbo/PTX vs M-VAC*	GC*[8]	PCG*§ vs GC*[8]
Phase	2	3	3	3	2	3
N	133	405	263	85	46	626
ORR, %	72	49.4 vs 45.7 (*P*=0.51)	64 vs 50 CR: 28 vs 12 pts (*P*=0.06)	28.2 vs 35.9 CR: 1 vs 5 pts (*P*=0.63)	41 CR: 10 pts	55.5 vs 43.6 (*P*=0.0031)
mPFS, mos	8	7.7 vs 8.3 (*P*=0.407)	9.5 vs 8.1 (*P*=0.017)	5.2 vs 8.7 (*P*=0.24)	5.5‖	8.3 vs 7.6 (*P*=0.113)
mOS, mos	13.3	14 vs 15.2 (*P*=0.66)	15.1 vs 14.9 (HR=0.76)	13.8 vs 15.4 (*P*=0.65)	14.3	15.8 vs 12.7 (*P*=0.075)
5-yr OS, %	18 (4-yr)	13 vs 15.3 (*P*=0.526)	21.8 vs 13.5 (*P*=0.042)	NR‡	NR	NR
Grade 3-4 AEs (top 3), %	Leukocyte count: 58 Nadir sepsis: 25 Platelets: 21	Neutropenia: 71.1 vs 82.3 Thrombocytopenia: 57 vs 20.6 Anemia: 27 vs 17.6	Platelets: 22 vs 17 WBC: 20 vs 62 Mucositis: 10 vs 17	Neutropenia: 29 vs 67 Anemia: 5 vs 38 Thrombocytopenia: 10 vs 21	Segmented neutrophils: 74 Platelet: 65 WBC: 53	Neutropenia: 64.3 vs 50.5 Thrombocytopenia: 34.5 vs 52.1 Hemoglobin: 22.5 vs 25.6
AEs leading to discontinuation, %	NA	NA	NA	9 vs 17	8	14.6 vs 15.7
Tx-related death, n	4	1% vs 3%	1 vs 1	1 vs 1	NA	6 vs 3

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První linie paliativní léčby mUC: **cisplatina unfit- chemoterapie**

	EORTC 30986[1]	Dreicer 2004[2]	Galsky 2007[3]
Therapies	GEM+carbo vs M-CAVI	carbo+PTX vs M-VAC	DOX+GEM → PTX+carbo
Phase	2/3	3	2
N	238	85	25
ORR, %	41.2 vs 30.3 (*P*=0.08)	28.2 vs 35.9 CR:1 vs 5 pts (*P*=0.63)	56
mPFS, mo	5.8 vs 4.2 (HR=1.04)	5.2 vs 8.7 (*P*=0.24)	NR
mOS, mo	9.3 vs 8.1 (*P*=0.64)	13.8 vs 15.4 (*P*=0.65)	15
5-yr OS, %	NR	NR	NR
Grade 3-4 AEs (top 3), %	Neutropenia: 52.5 vs 63.5 Leucopenia: 44.9 vs 46.6 Thrombocytopenia: 48.3 vs 19.4	Neutropenia: 29 vs 67 Anemia: 5 vs 38 Thrombocytopenia: 10 vs 21	Neutropenia: 28 Anemia: 16 Thrombosis: 16 Thrombocytopenia: 8 Nausea: 8 Vomiting: 8
AEs leading to discontinuation, %	21.0 vs 21.8	9 vs 17	2
Tx-related death, n	2 vs 4	1 vs 1	NA

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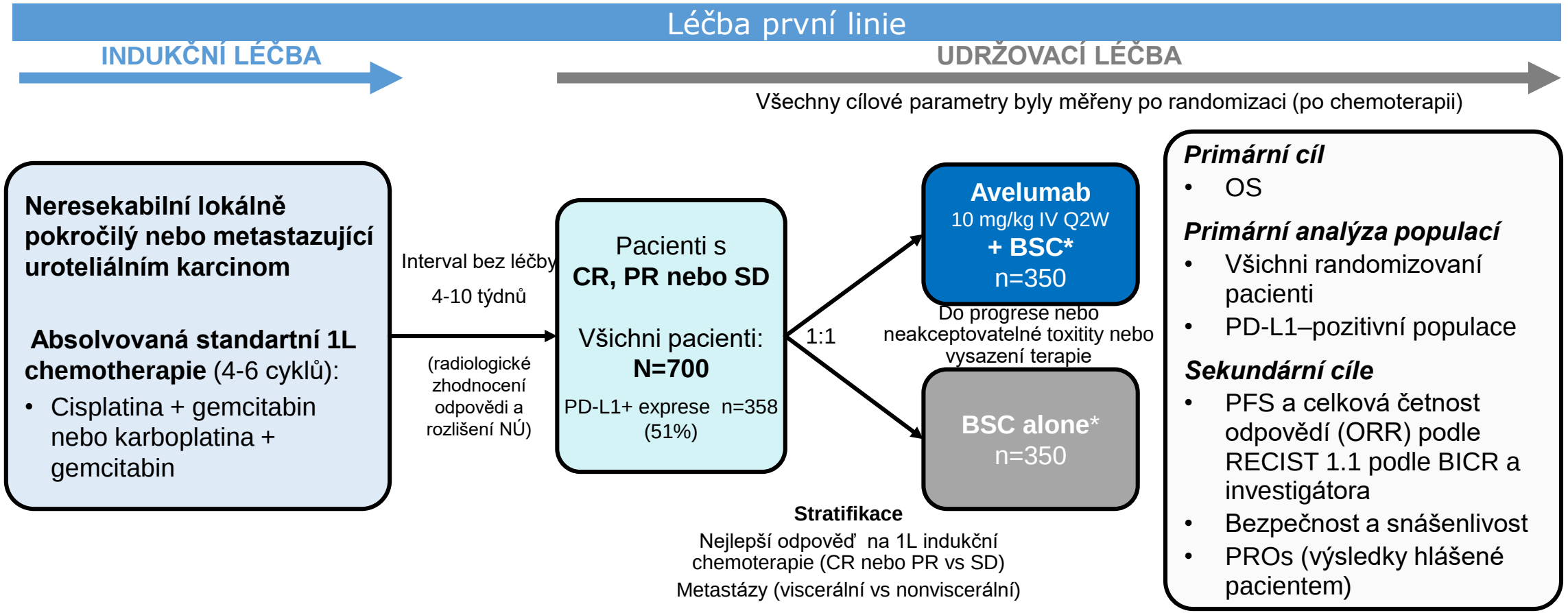
PO CHT dle ASCO 2020:
Udržovací léčba avelumab + nejlepší podpůrná léčba (BSC) versus BSC samotná po chemoterapii na bázi platiny v první linii pokročilého uroteliálního karcinomu:
JAVELIN Bladder 100 phase III výsledky

JAVELIN Bladder 100 režim



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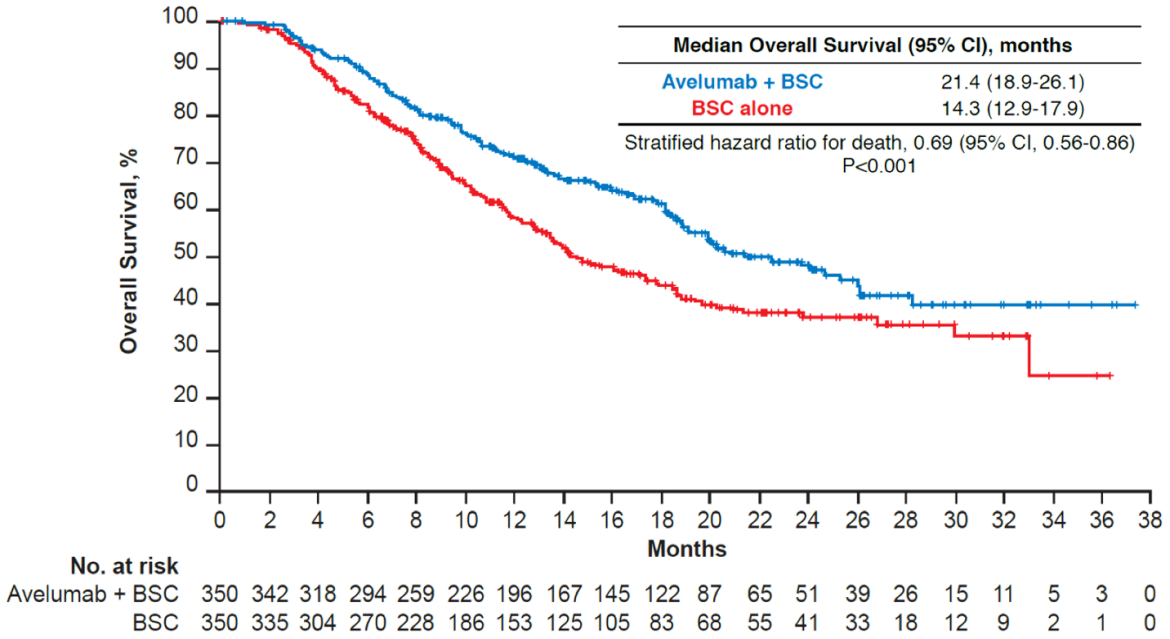
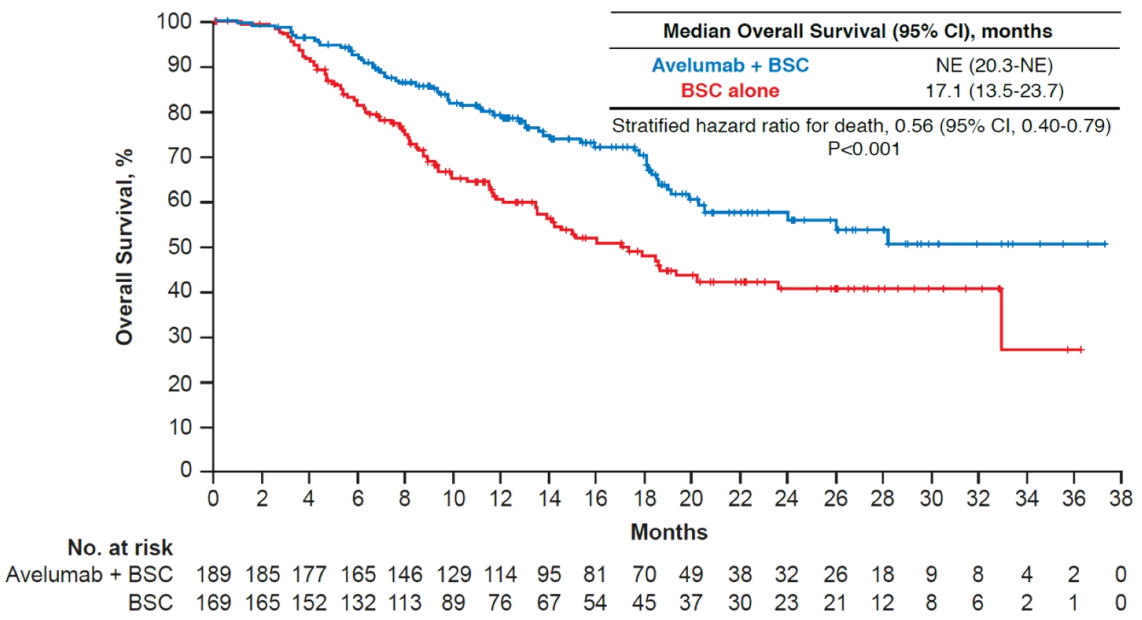
JAVELIN Bladder 100 phase III výsledky

OS v celkové populaci



OS v PD-L1–pozitivní populaci



BAVENCIO je první imunoterapií, která v klinické studii s inovativním designem (indukce+ maintenance) prokázala statisticky významné zlepšení v parametru OS v léčbě první linie u pacientů s pokročilým uroteliálním karcinomem.

Režim dle designu studie Javelin Bladder 100 je aktuálně doporučený NCCN i ESMO.

První linie paliativní léčby mUC: **cisplatina unfit- imunoterapie**

	KEYNOTE-052[1]			IMvigor210 (Cohort 1)[4]		
Regimens	Pembrolizumab			Atezolizumab		
Ph	2[2]			2		
N	370	251	110	119	32	80
Patient subgroups	Cisplatin-ineligible	PD-L1 CPS < 10	PD-L1 CPS ≥ 10	All-comers	PD-L1 expression of ≥5% in ICs	PD-L1 expression of ≥1% in ICs
ORR, % (95% CI)	**29 (24–34)***	21 (16–26)	47 (38–57)	**22.7 (15.5–31.3)†**	**28.1 (13.8–46.8)†**	**23.8 (15.0–34.6)†**
mPFS, mo (95% CI)	2.3 (2.1–3.4)*	NA	NA	2.7 (2.1–4.2)†	4.1 (2.3–11.8)†	2.9 (2.1–5.4)†
mOS, mo (95% CI)	11.0 (10.0–13.6)*	10 (8–12)	19 (12–NR)	15.9 (10.4–NE)	12.3 (6.0–NE)	14.1 (9.2–NE)
Grade 3-4 AEs (top 3), %	NA[3]			Fatigue: 3, AST increased: 3, ALT increased: 3[5]		
AEs leading to discontinuation, %	10[3]			9[5]		
Tx-related death, n	1[3]			1[5]		

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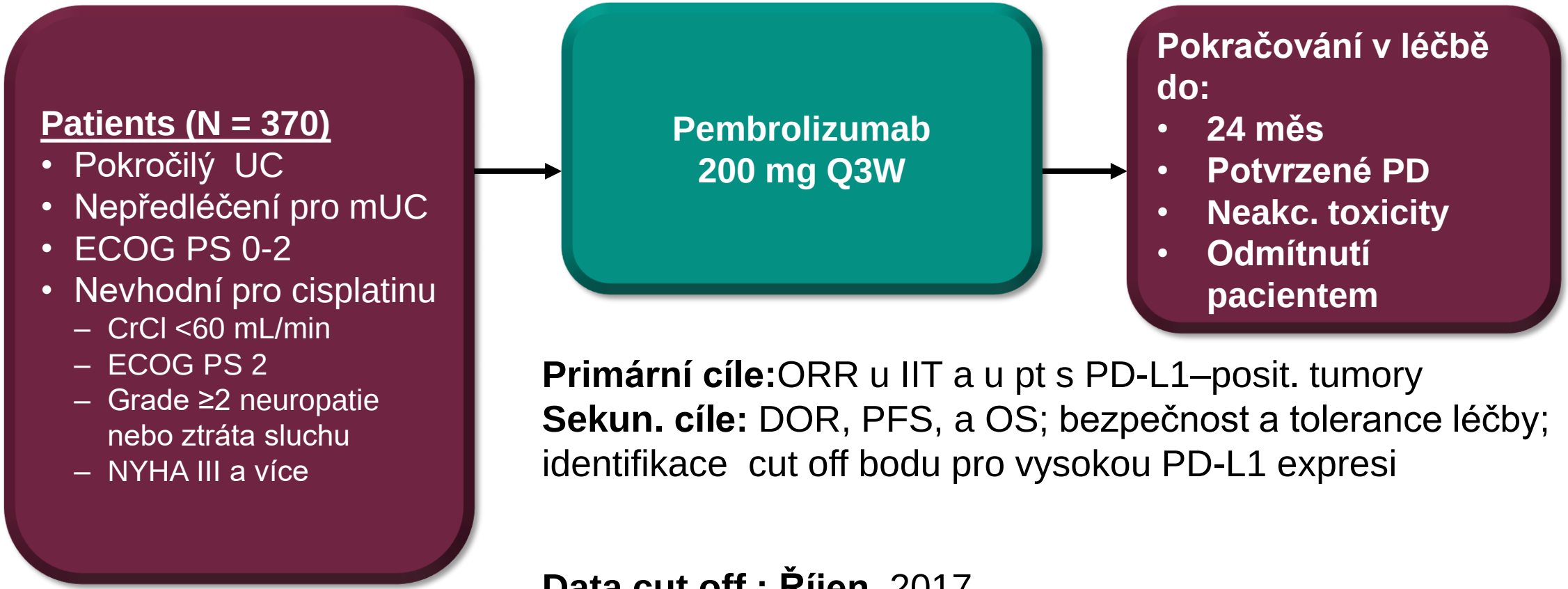
Nádory močového měchýře a pembrolizumab, první linie léčby mUC, KEYNOTE 052- studie II.fáze



Primární cíle:ORR u IIT a u pt s PD-L1–posit. tumory
Sekun. cíle: DOR, PFS, a OS; bezpečnost a tolerance léčby; identifikace cut off bodu pro vysokou PD-L1 expresi

Data cut off : Říjen, 2017

Medián follow-up: 11.5 months (0.1 - 31.3 m)

Vuky et al, JCO 2018

Nádory močového měchýře a pembrolizumab, první linie léčby mUC, KEYNOTE 052, charakteristika souboru pt

Characteristic, n (%)	N = 370
Age, median (range), y	74 (34-94)
≤64 years	68 (18)
65-74 years	123 (33)
75-84 years	139 (38)
≥85 years	40 (11)
Men	286 (77)
ECOG performance status[a]	
0	80 (22)
1	134 (36)
2	155 (42)
3	1 (<1)
Primary tumor location	
Upper tract	69 (19)
Lower tract	300 (81)
Metastases location[c]	
Lymph node only	51 (14)
Visceral disease	315 (85)
Liver metastases	77 (21)

Characteristic, n (%)	N = 370
Prior adjuvant/neoadjuvant platinum-based chemotherapy[d]	37 (10)
Reasons for cisplatin ineligibility	
Renal dysfunction	183 (50)
ECOG performance status 2	120 (32)
ECOG performance status 2 and renal dysfunction	34 (9)
Other reasons[e]	33 (9)

Characteristic, n (%)	N = 370
PD-L1 CPS ≥ 10	110 (32%)
PD- L1 CPS < 10	251 (68%)

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Vuky et al, JCO 2018

Nádory močového měchýře a pembrolizumab, první linie léčby mUC, KEYNOTE 052, ORR u IIT

	Total Population	
	n	**% (95% CI)**
Objective response rate	107	**29%** (24.3-33.8)
Complete response	30	8 (5.5-11.4)
Partial response	77	21 (16.8-25.3)
Disease control rate	174	47 (41.8-52.3)
Stable disease	67	18 (14.3-22.4)
Progressive disease	156	42 (37.1-47.4)
No assessment	31	8 (5.8-11.7)
Not evaluable	9	2 (1.1-4.6)

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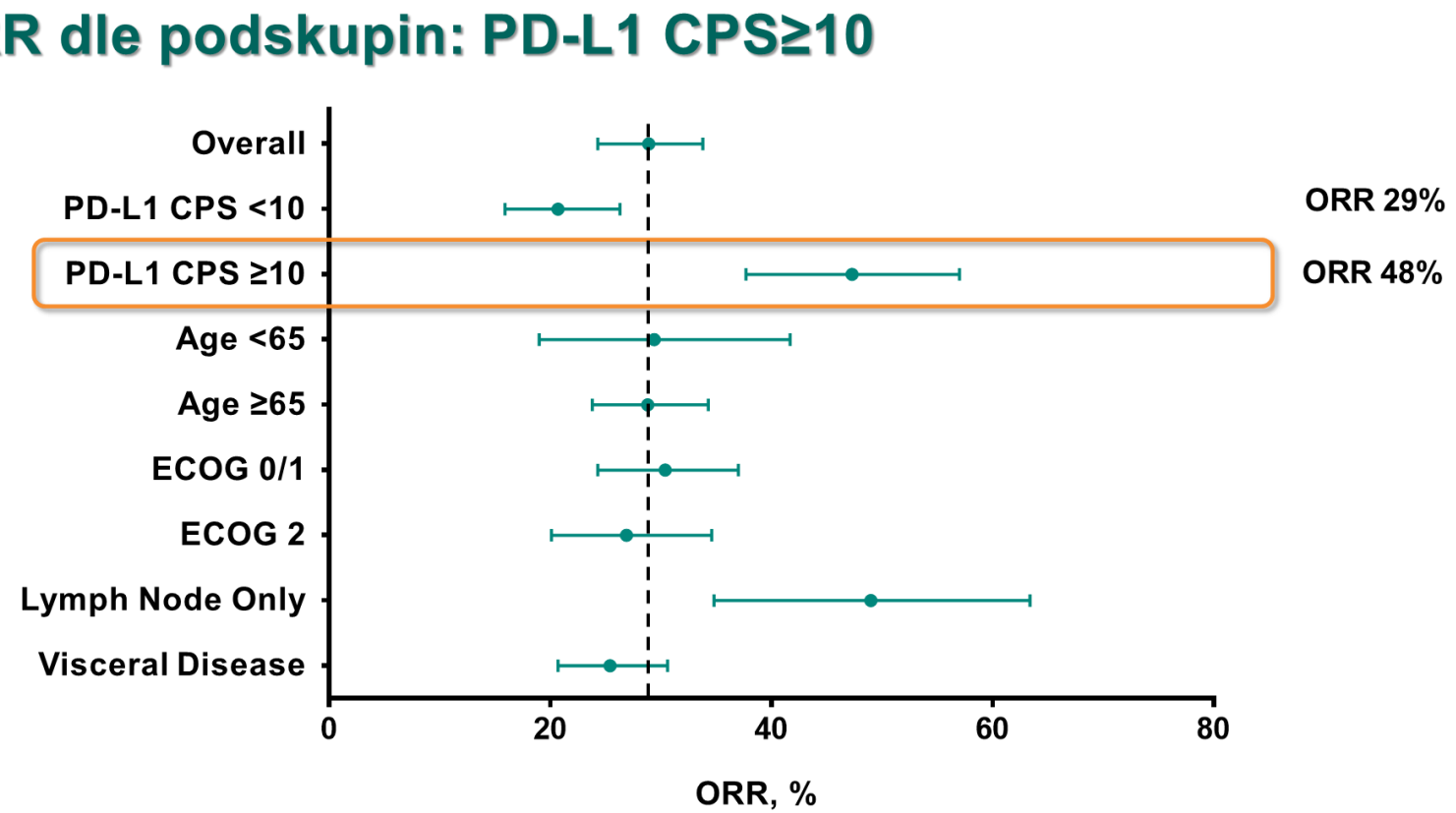
Vuky et al, JCO 2018

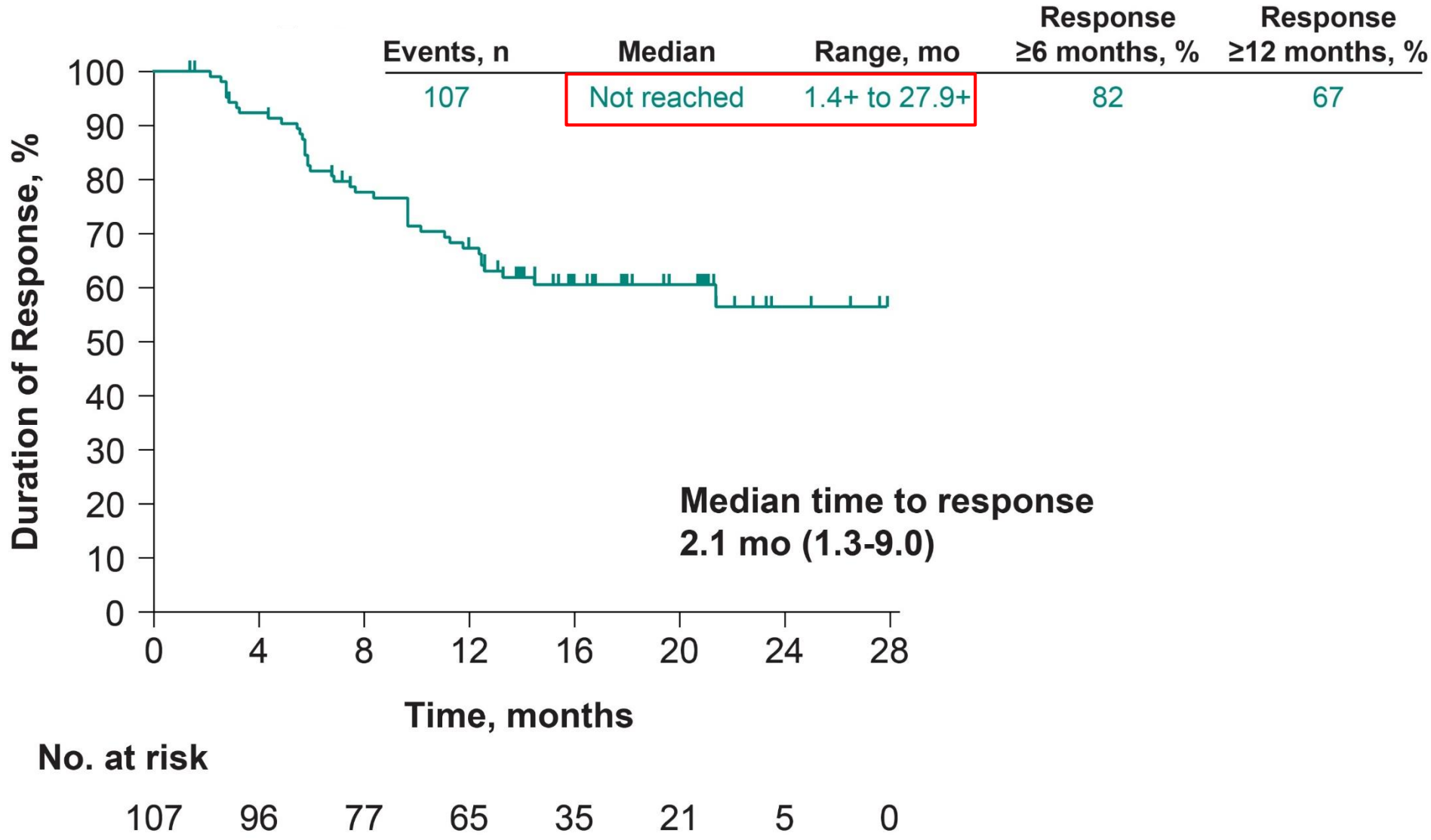
Nádory močového měchýře a pembrolizumab, první linie léčby mUC, KEYNOTE 052, PD-L1 exprese a ORR



Data cutoff: Nov 30, 2017.

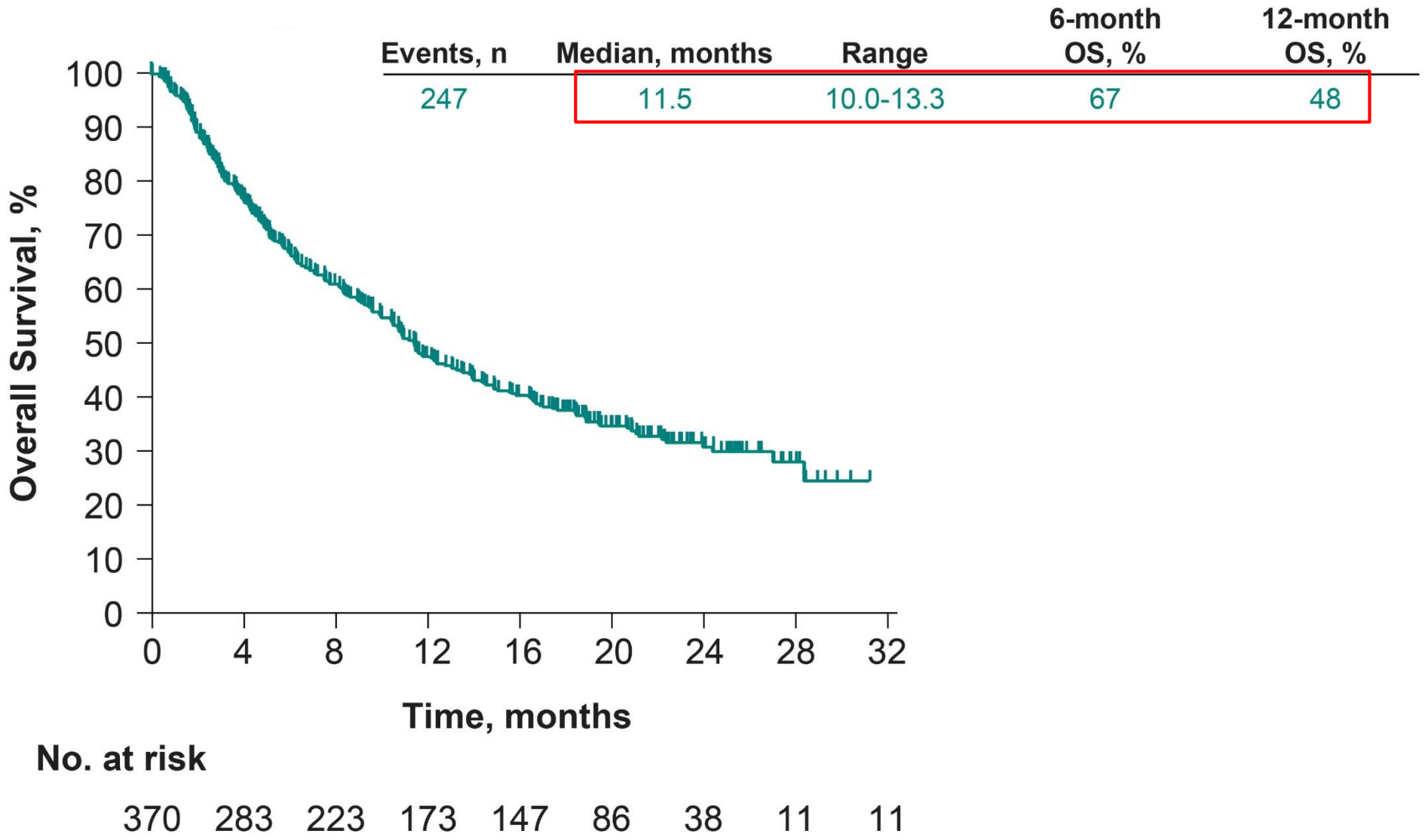
Vuky et al, JCO 2018

Nádory močového měchýře a pembrolizumab, první linie léčby mUC, KEYNOTE 052, DOR a doba do léčebné odpovědi



Vuky et al, JCO 2018

Nádory močového měchýře a pembrolizumab, první linie léčby mUC, KEYNOTE 052, OS



Data cutoff: Nov 30, 2017.

Nádory močového měchýře a pembrolizumab, první linie léčby mUC, KEYNOTE 052, OS dle podskupin

	N	Events, n (%)	Median OS (95% CI), months
All patients	370	247 (66.8)	11.5 (10.0-13.3)
PD-L1 subgroup			
PD-L1 CPS <10	251	186 (74.1)	10.0 (7.8-11.6)
PD-L1 CPS ≥10	**110**	**57 (51.8)**	**18.5 (12.2-NR)**
Age			
<65 years	68	41 (60.3)	15.7 (6.9-NR)
≥65 years	302	206 (68.2)	11.9 (9.7-12.8)
ECOG performance status			
0/1	214	134 (62.6)	13.1 (11.0-16.8)
2	156	113 (72.4)	9.7 (5.7-11.6)
Metastases location			
Lymph node only	51	22 (43.1)	NR (12.4-NR)
Visceral disease	315	223 (70.8)	10.8 (9.0-11.8)

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Vuky et al, JCO 2018

Nádory močového měchýře a pembrolizumab, první linie léčby mUC, NUL

	All n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
Any	**107 (29)**	**24 (9)**	**49 (13)**	**29 (8)**	**5 (1)**
Hypothyroidism	42 (11)	9 (2)	33 (9)	0	0
Pneumonitis	15 (4)	4 (1)	6 (2)	5 (1)	0
Hyperthyroidism	11 (3)	8 (2)	3 (<1)	0	0
Colitis	10 (3)	2 (<1)	2 (<1)	5 (1)	1 (<1)
Adrenal insufficiency	6 (2)	0	1 (<1)	3 (<1)	2 (<1)
Hepatitis	3 (<1)	0	0	3 (<1)	0
Thyroiditis	3 (<1)	0	2 (<1)	1 (<1)	0
Type 1 diabetes mellitus	3 (<1)	0	1 (<1)	2 (<1)	0
Autoimmune hepatitis	2 (<1)	0	0	2 (<1)	0
Dermatitis bullous	2 (<1)	1 (<1)	1 (<1)	0	0
Diabetic ketoacidosis	2 (<1)	0	0	1 (<1)	1 (<1)
Myocarditis	2 (<1)	0	0	1 (<1)	1 (<1)
Pruritus	2 (<1)	0	0	2 (<1)	0
Rash	2 (<1)	0	0	2 (<1)	0
Tubulointerstitial nephritis	2 (<1)	0	0	2 (<1)	0

Vuky et al, JCO 2018

Druhá a vyšší linie paliativní léčby

- Taxany, vi
- **Chemoter**

Vinflunin

Table 1.

Observations reporting on clinical outcome of VFL in daily clinical practice since the drug's approval in 2009.

Author	Number of observed patients	OS/PFS (months)
Pistamaltzian *et al.* [2016]	$n = 71$, retrospective study	11.9/6.9
Moriceau *et al.* [2015]	$n = 19$, retrospective study	4.0/2.9
Medioni *et al.* [2016]	$n = 134$, retrospective study	8.2/4.2
Hegele *et al.* [2014]	$n = 21$, retrospective study	6.2/4.4
Retz *et al.* [2015]	$n = 77$, prospective study	7.7/–
Castellano *et al.* [2014]	$n = 102$, prospective study	10.0/3.9
Palacka *et al.* [2014]	$n = 16$, prospective study	5.2/2.3
Summarized	$n = 440$, prospective and retrospective observations	7.6/4.1
Bellmunt *et al.* [2009]	$n = 259$, phase III trial	6.9/3.0

OS, overall survival; PFS, progression-free survival.

Odpovědi na léčbu: PR 8,6%, SD 46%

Regimens				
Ph				
N				
ORR, %				
mPFS, mo				
mOS, mo				
Grade 3-4 AEs (top 3), %				
AEs leading to discontinuation, %				
Tx-related death, n				

Druhá a vyšší linie paliativní léčby

- Taxany, vinflunin a zase IMUNOTERAPIE
- **Imunoterapie**: pembrolizumab, atezolizumab, nivolumab … a další

	KEYNOTE-045[1,2,3]			IMvigor210 (cohort 2)[4,5]			CheckMate 275[6,7]			Study 1108[8,9]			JAVELIN[10]		
Regimens	Pembrolizumab vs chemotherapy			Atezolizumab			Nivolumab			Durvalumab			Avelumab‡‡		
Ph	3			2			2			1/2			1		
N	270 vs 272			310			270			191			161		
Patient subgroups	ITT population	PD-L1 CPS < 10	PD-L1 CPS ≥ 10	All-comers	PD-L1 expression of ≥ 5% in ICs	PD-L1 expression of ≥ 1% in ICs	All-comers	Tumor PD-L1 expression of < 1%	Tumor PD-L1 expression of ≥ 1%	All-comers	PD-L1 expression of ≥ 1% in ICs	PD-L1 low or negative	All-comers	PD-L1 expression of ≥ 5% in ICs	PD-L1 expression of < 5% in ICs
ORR, % (95% CI)	21.1* vs 11.4* ($P^{\dagger}$=0.001)	NA[1]	21.6 vs 6.7[3]	15.8 (11.9, 20.4)	28.0 (19.5, 37.9)	19.3 (14.2, 25.4)	20 (16, 26)	16 (10, 23)	26 (18, 34)	17.8 (12.7, 24.0)	27.4 (18.7, 37.5)	4.1 (0.9, 11.5)	17 (11, 24)	24 (14, 36)	13 (7, 23)
mPFS, mo (95% CI)	2.1* vs 3.3* ($P^{\dagger}$=0.416) ($HR^{\S}$=0.98)	NA[1]	NA[1]	NA[3]			2.0 (1.9, 2.6)	1.9 (1.8, 2.0)	3.6 (1.9, 3.7)	1.5 (1.4, 1.9)	2.1 (1.4, 2.8)	1.4 (1.3, 1.5)	6.3 wks (6.0, 10.1)	11.9 wks (6.1, 18.0)	6.1 wks (5.9, 8.0)
mOS, mo (95% CI)	10.3 vs 7.4 ($P^{\dagger}$=0.002) ($HR^{\S}$=0.73)	NA**	NA**	NA[3,4††]			8.6 (6.05, 11.27)	5.9 (4.37, 8.08)	11.6 (9.10, NE)	18.2 (8.1, NE)	20.0 (11.6, NE)	8.1 (3.1, NE)	6.5 (4.8, 9.5)	8.2 (5.7, 13.7)	6.2 (4.3, 14.0)
Grade 3-4 TRAEs , %	Grade 3–5: 15.0 vs 49.4			16			23			6.8			8		
TRAEs leading to discontinuation, %	5.6 vs 11.0			NA			NA			1.6			6		
Tx-related death, n	1.5 vs 1.6			0			1			1			<1		

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Nádory močového měchýře a pembrolizumab, druhá linie léčby mUC, KEYNOTE 045, design studie- III.fáze

Key Eligibility Criteria

- Urothelial carcinoma of the renal pelvis, ureter, bladder, or urethra
- Transitional cell predominant
- PD after 1 or 2 lines of platinum-based chemotherapy or recurrence <12 months after perioperative platinum-based therapy
- ECOG performance status 0-2
- Tumor sample for biomarker assessment[a]

Stratification Factors

- ECOG performance status (0/1 vs 2)
- Hemoglobin level (<10 vs ≥10 g/dL)
- Liver metastases (yes vs no)
- Time from last chemotherapy dose (<3 vs ≥3 months)

R (1:1)
N = 542

N = 270

Pembrolizumab
200 mg IV Q3W

N = 272

Paclitaxel 175 mg/m² Q3W
or
Docetaxel 75 mg/m² Q3W
or
Vinflunine 320 mg/m² Q3W

- Dual primary end points: OS and PFS[b]
- Key secondary end points: ORR, DOR, safety
- Response: RECIST v1.1 by blinded, independent central review
- Unselected and biomarker-selected patients
- Data cutoff for this analysis was October 26, 2017

- **Median follow-up, 27.7 months**

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Fradet et al, Ann Oncology 2018

Nádory močového měchýře a pembrolizumab, druhá linie léčby mUC, KEYNOTE 045, charakteristika souboru

n (%)	Pembro N = 270	Chemo N = 272
Age, median (range), y	66 (29-88)	65 (26-84)
Men	200 (74.1)	202 (74.3)
Upper tract disease	38 (14.1)	37 (13.6)
Lower tract disease	232 (85.9)	235 (86.4)
ECOG performance status[a]		
0	120 (44.4)	106 (39.0)
1	142 (52.6)	158 (58.1)
2	3 (1.1)	4 (1.5)
Visceral disease	241 (89.3)	235 (86.4)
Disease in lymph node only	28 (10.4)	37 (13.6)
Liver metastases	91 (33.7)	95 (34.9)
Hemoglobin <10 g/dL[b]	43 (15.9)	44 (16.2)
PD-L1 CPS ≥10	74 (27.4)	90 (33.1)

n (%)	Pembro N = 270	Chemo N = 272
Time since completion of most recent therapy		
≥3 months	167 (61.9)	168 (61.8)
<3 months	103 (38.1)	104 (38.2)
Setting of most recent therapy		
Neoadjuvant	19 (7.0)	22 (8.1)
Adjuvant	12 (4.4)	31 (11.4)
First line	184 (68.1)	158 (58.1)
Second line	55 (20.4)	59 (21.7)
Third line	0	2 (0.7)
Risk factors[c]		
0	54 (20.0)	45 (16.5)
1	97 (35.9)	97 (35.7)
2	66 (24.4)	80 (29.4)
3/4	45 (16.7)	45 (16.5)

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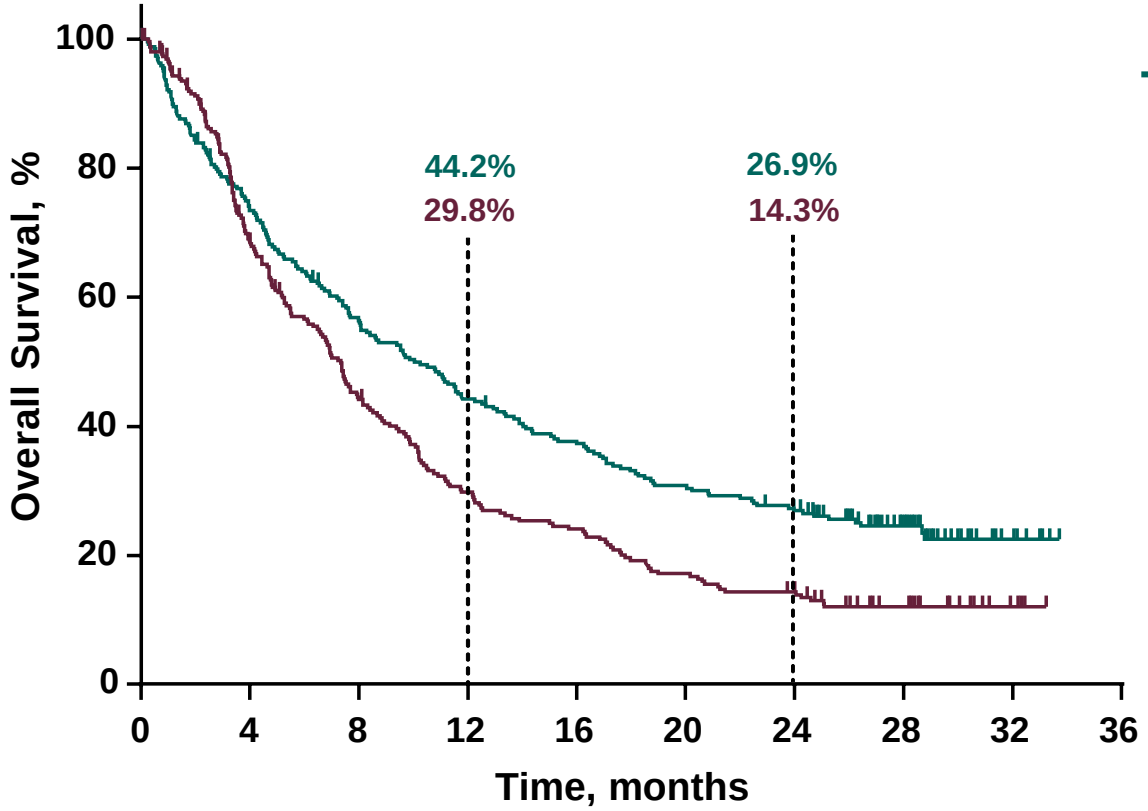
Fradet et al, Ann Oncology 2018

Nádory močového měchýře a pembrolizumab, druhá linie léčby mUC, KEYNOTE 045, OS



No. at risk										
Pembrolizumab	270	195	148	116	98	80	67	33	7	0
Chemotherapy	272	173	109	73	59	42	34	18	4	0

	Events, n	HR (95% CI)[a]	*P*[b]
Pembro	200	0.70 (0.57-0.85)	0.00015
Chemo	219		

Median (95% CI):

10.1 months (8.0-12.3 months)

7.3 months (6.1-8.1 months)

- **60.6% pacientů v rameni s chemoterapií bylo následně léčeno anti PD-1/PD-L1 léčbou** (přeživší 24 měsíců a více)

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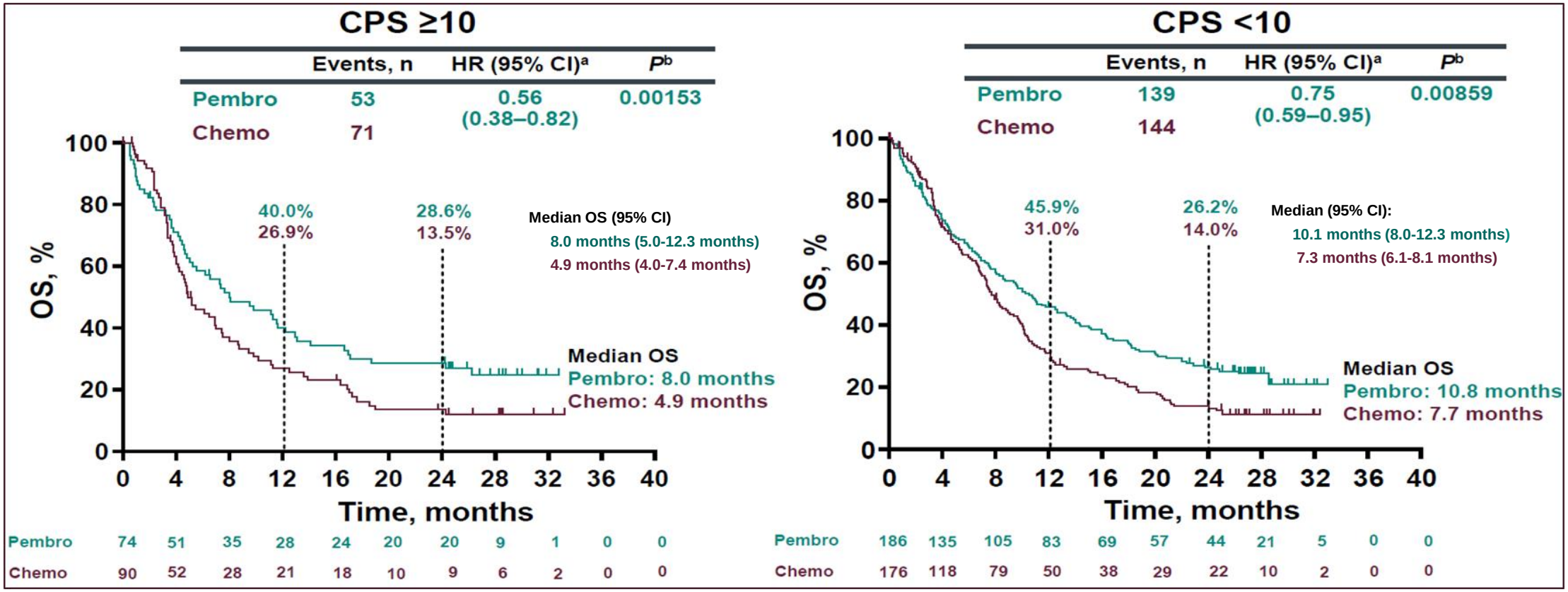
Fradet et al, Ann Oncology 2018

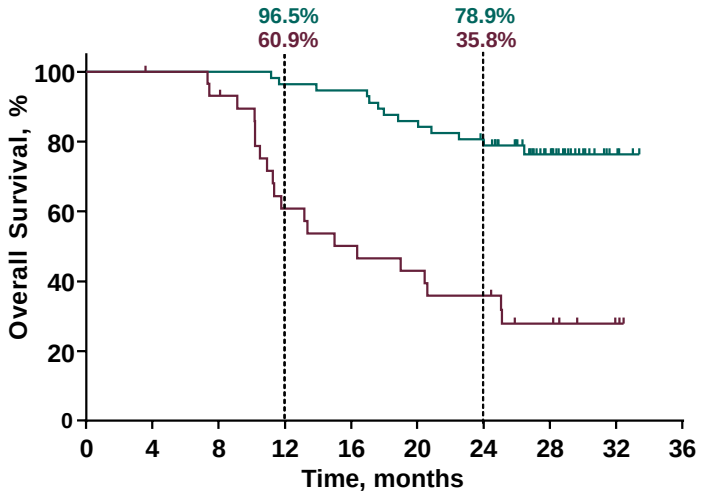
Nádory močového měchýře a pembrolizumab, druhá linie léčby mUC, KEYNOTE 045, OS dle PD-L1



Fradet et al, Ann Oncology 2018

Nádory močového měchýře a pembrolizumab, druhá linie léčby mUC, KEYNOTE 045, OS dle odpovědi na léčbu

Responders CR + PR (N =87)

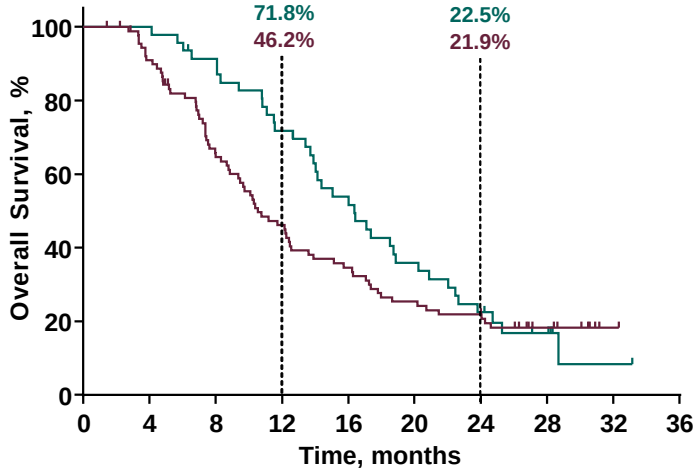


No. at risk

Pembrolizumab	57	57	57	55	54	49	43	22	4	0
Chemotherapy	30	29	27	17	14	12	10	6	2	0

Median OS
Pembro: NR (95% CI, NR–NR)
Chemo: 16.4 months (95% CI, 11.3-25.1 months)
HR: 0.14 (95% CI, 0.06-0.33), *P* < 0.00001

SD (N = 139)

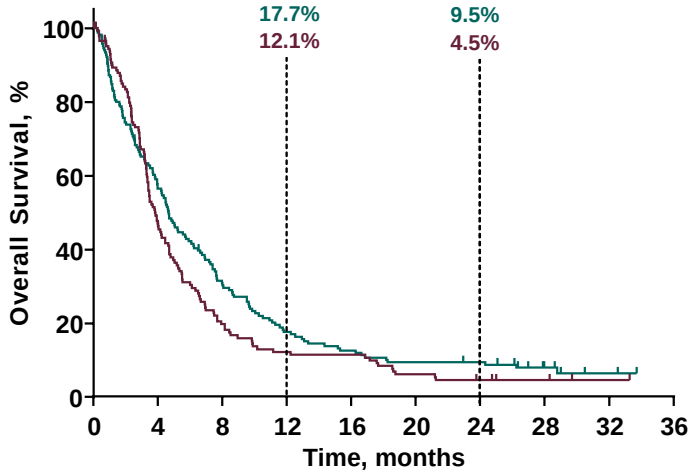


No. at risk

Pembrolizumab	47	47	42	33	24	16	10	5	1	0
Chemotherapy	92	81	56	40	30	22	19	9	1	0

Median OS
Pembro: 16.4 months (95% CI, 13.7-18.9 months)
Chemo: 10.5 months (95% CI, 8.8-12.6 months)
HR: 0.77 (95% CI, 0.51-1.17), *P* = 0.10404

Nonresponders PD + Not Assessed + Not Evaluable (N = 316)



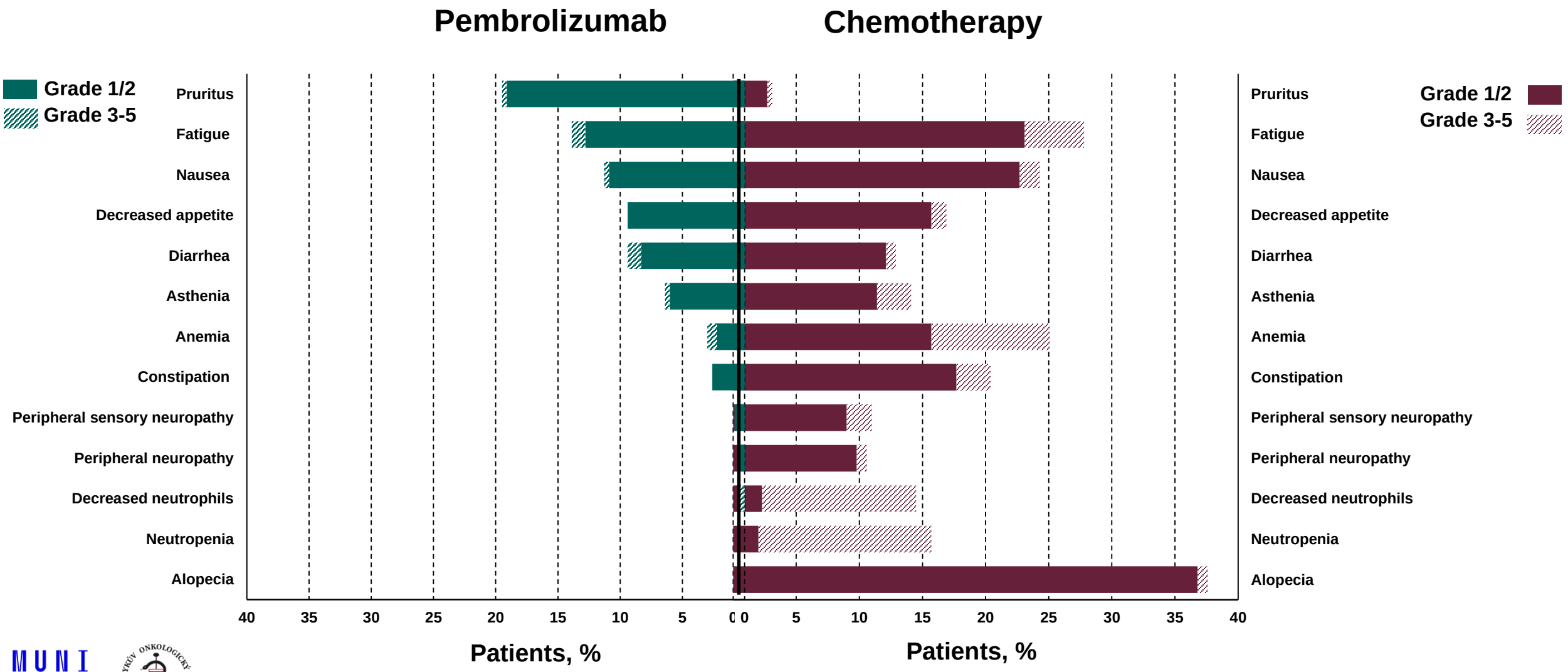
No. at risk

Pembrolizumab	166	91	49	28	20	15	14	6	2	0
Chemotherapy	150	63	26	16	15	8	5	3	1	0

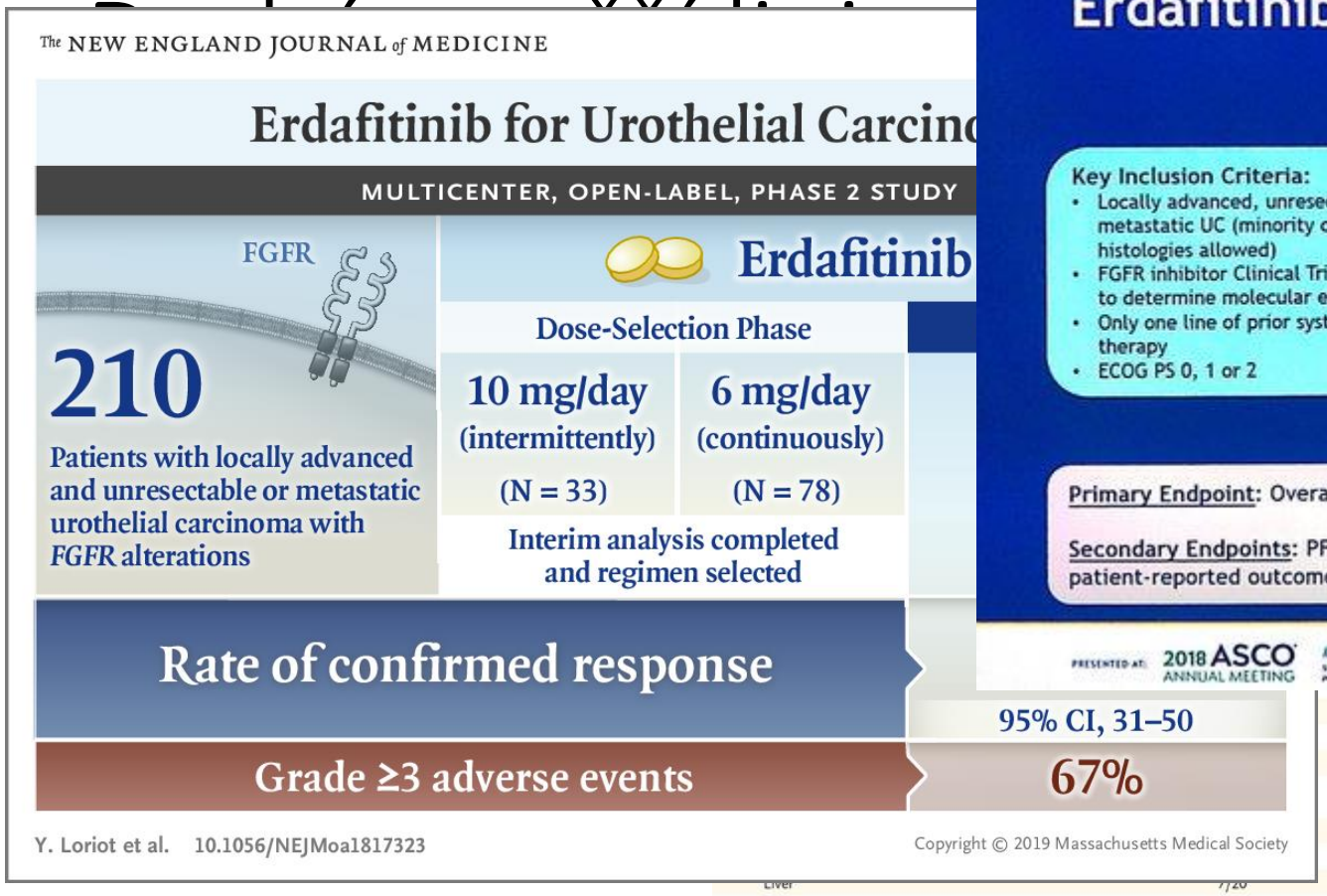
Median OS
Pembro: 4.7 months (95% CI, 3.9-5.9 months)
Chemo: 3.8 months (95% CI, 3.3-4.4 months)
HR: 0.85 (95% CI, 0.66-1.09), *P* = 0.09751

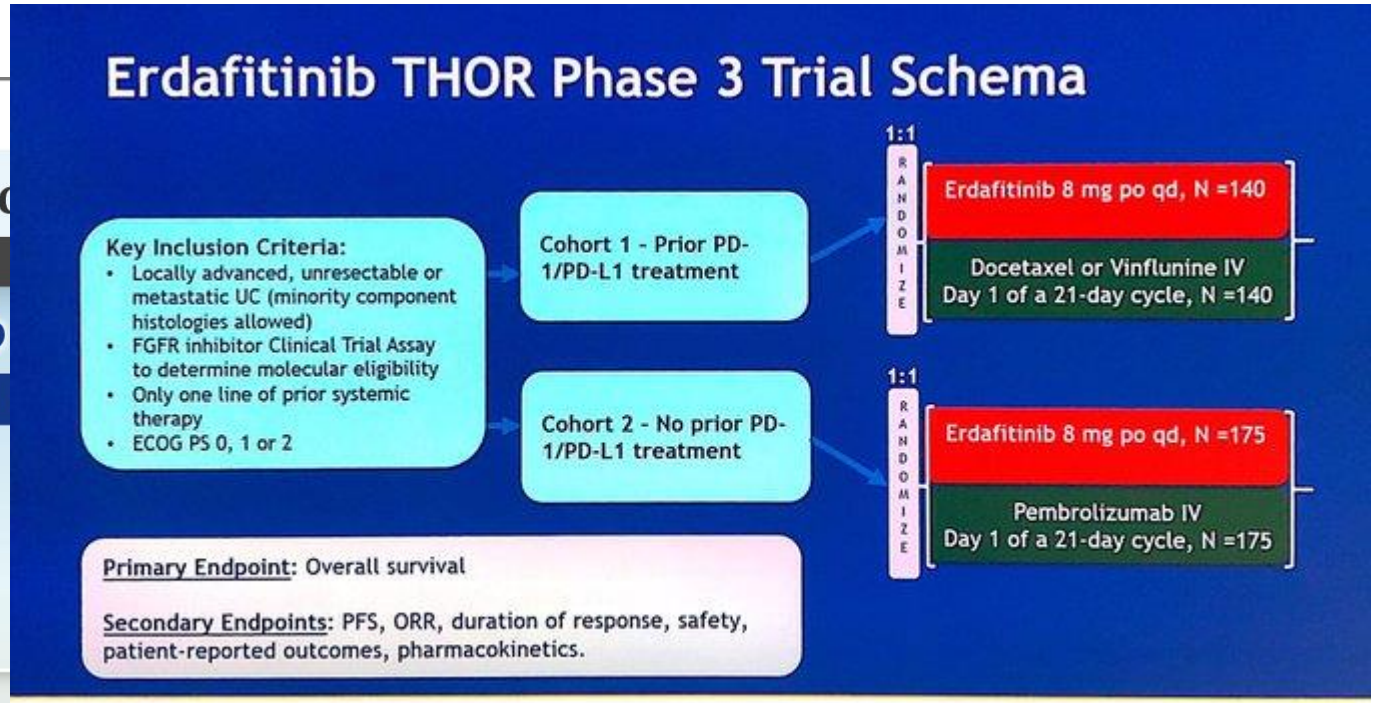
Fradet et al, Ann Oncology 2018

Nádory močového měchýře a pembrolizumab, druhá linie léčby mUC, KEYNOTE 045, NUL (více než 10% pt)



Fradet et al, Ann Oncology 2018





PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18 PRESENTED BY: Evan Y. Yu, M.D. 16

		38 (20–56)
		60 (30–90)
		50 (1–99)
		38 (28–49)
		48 (26–69)
Liver	7/26	35 (14–56)
Lung	23/57	40 (28–53)
Lymph node only	4/12	33 (7–60)
Upper tract disease‡	10/23	43 (23–64)
Lower tract disease§	30/76	39 (29–51)
Absent	10/21	48 (26–69)
Response according to daily dose of erdafitinib — no./total no.		
8 mg	20/58	34 (22–47)
mg with dose escalation to 9 mg	20/41	49 (34–67)
Response according to genetic alteration — no./total no.		
FGFR3 mutation	36/74	49 (37–60)
FGFR2/3 fusion	4/25	16 (2–30)

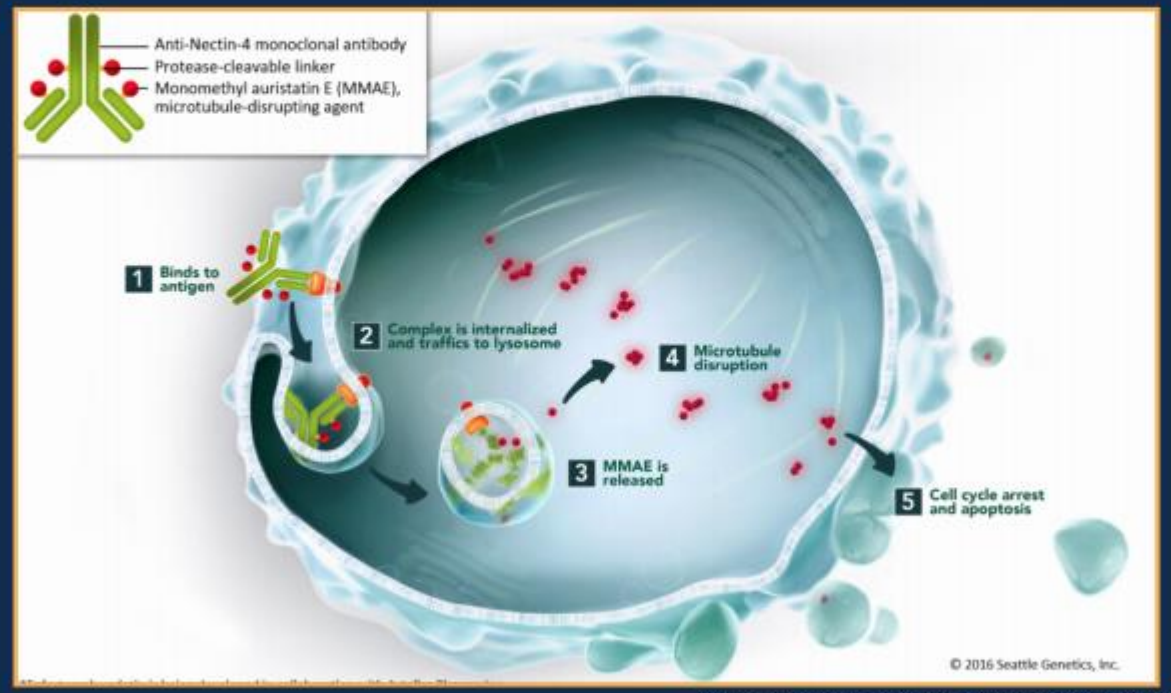
,4 měsíce,

- Mediány PFS a OS z ěsíce

Loriot et al., NEJM 2019

Druhá a vyšší linie paliativní léčby, Enfortumab vedotin, PADCEV®

Enfortumab Vedotin: Proposed Mechanism of Action



Enfortumab Vedotin is being co-developed by Seattle Genetics, Inc. and Astellas Pharma Inc.

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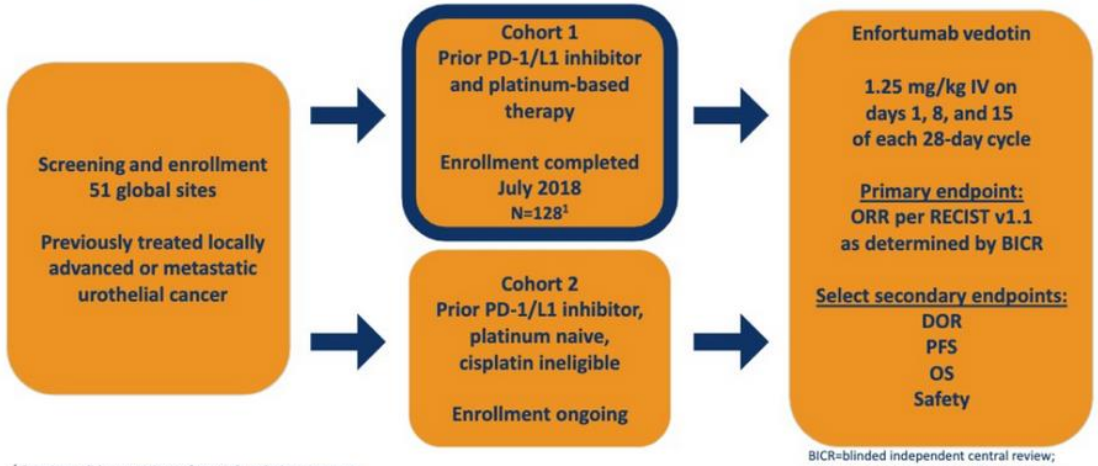
MASARYKŮV ONKOLOGICKÝ ÚSTAV

Druhá a vyšší linie paliativní léčby, Enfortumab vedotin, studie fáze II- kohorta 1 a 2 - po selhání imunoterapie s nebo bez předchozí chemoterapií

EV-201: Single-Arm, Pivotal Phase 2 Trial



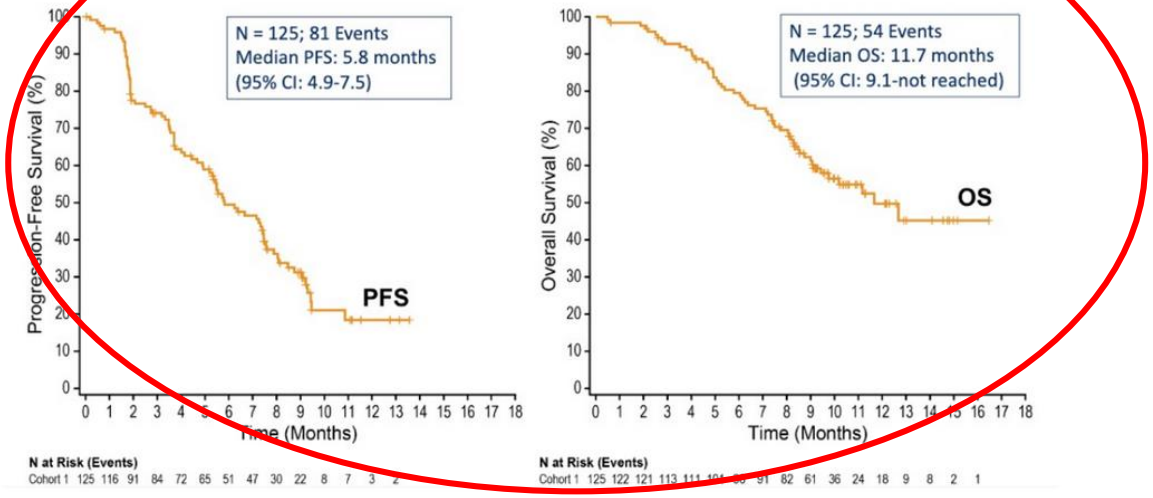
[1] 3 patients did not receive enfortumab vedotin treatment: one each due to clinical deterioration, patient decision, and low hemoglobin after enrollment

BICR=blinded independent central review; DOR=duration of response; ORR=objective response rate; OS=overall survival; PFS=progression-free survival

	Patients (N=125)
Male sex, n (%)	88 (70)
Age, years	
Median (min, max)	69 (40, 84)
≥75 years, n (%)	34 (27)
ECOG PS of 1, n (%)	85 (68)
Primary tumor location, n (%)	
Bladder/other	81 (65)
Upper tract	44 (35)
Number of prior systemic therapies[1], median (range)	3 (1, 6)
≥2 Bellmunt adverse prognostic factors	52 (42)
Metastasis sites, n (%)	
Lymph nodes only	13 (10)
Visceral disease	112 (90)
Liver	50 (40)
PD-L1 status by combined positive score[2]	
<10	78/120 (65)
≥10	42/120 (35)

ORR per RECIST v 1.1 assessed by BICR	Patients (N=125) n (%)
Confirmed objective response rate	55 (44)
95% confidence interval[1]	(35.1, 53.2)
Best overall response per RECIST v. 1.1, n (%)	
Complete response	15 (12)
Partial response	40 (32)
Stable disease	35 (28)
Progressive disease	23 (18)
Not evaluable[2]	12 (10)

EV-201: Cohort 1 Kaplan-Meier Estimates of Survival



Petrylak et al., ASCO 2019

Druhá a vyšší linie paliativní léčby, Enfortumab vedotin

Enfortumab vedotin and pembolizumab with or without chemotherapy vs chemotherapy alone in advanced urothelial cancer (EV302).

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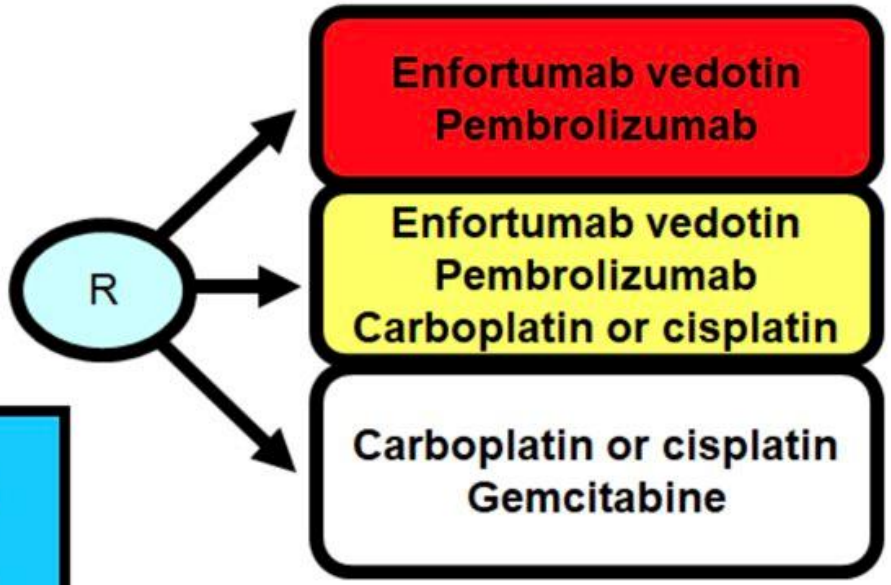
› 1,25

NCT04223856



- Frist line advanced UC
- Performance status 0-2
- N=1095
- Endpoints=PFS and OS
- Open label
- Start date: March 2020

!!!, 53,7%

Padcev Combination Shows Promise in Patients with Metastatic Bladder Cancer. Cure website. Published February 15, 2020. curetoday.com/articles/padcev-combination-shows-promise-in-patients-with-metastatic-bladder-cancer. Accessed February 19, 2020.

Děkuji za pozornost