

Grupo Português
Génito - Urinário



XXVIII Workshop

Urologia Oncológica

• EPIC SANA Marquês Hotel
LISBOA



A late recurrence of bladder cancer?

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DISCLOSURE OF INTEREST

- No conflict of interests.



66-year old woman

No allergies

PH: heavy smoker - 55 pack years

No family history of cancer

- SEP 2012:** Painless hematuria and pelvic pain
- NOV 2012:** TURBT - pT1 high grade urothelial carcinoma

- CT scan NOV 2012:**
 - Bladder wall thickening and left ureterohydronephrosis
- ECOG-0
- Fit for cisplatin





TURBT DEC 2012: pT2 high grade urothelial carcinoma, stage II

★ **Multidisciplinary tumour board DEC 2012: Neoadjuvante ChT > Surgery**

Neoadjuvant ChT: CDDP/GEM 4 cycles

**JUL 2013: Radical cystectomy with pelvic lymph node dissection – ypT2aN0 (0/15), R0
+ Ileal conduit diversion**

★ **Multidisciplinary tumour board AUG 2013: Surveillance**



2023?

CheckMate 274

Study design

- CheckMate 274 is a phase 3, randomized, double-blind, multicenter study of adjuvant nivolumab versus placebo in patients with high-risk MIUC

N = 709

Key inclusion criteria

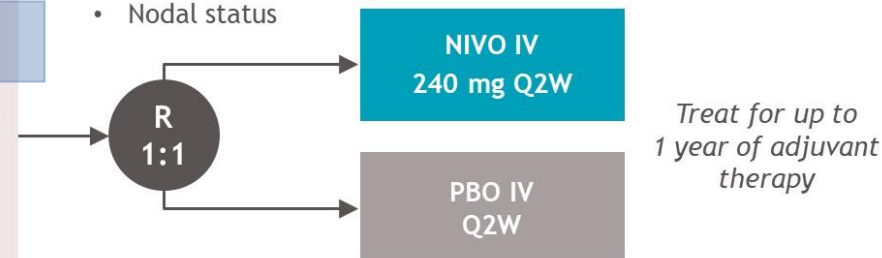
- Patients with ypT2-ypT4a or ypN+ MIUC who had neoadjuvant cisplatin chemotherapy
- Patients with pT3-pT4a or pN+ MIUC without prior neoadjuvant cisplatin chemotherapy and not eligible/refuse adjuvant cisplatin chemotherapy
- Radical surgery within the past 120 days
- Disease-free status within 4 weeks of dosing

Minimum follow-up, 5.9 months

Median follow-up in ITT population, 20.9 months (NIVO) and 19.5 months (PBO)

Stratification factors

- PD-L1 status (<1% vs \geq 1%)^a
- Prior neoadjuvant cisplatin-based chemotherapy
- Nodal status



Primary endpoints: DFS in ITT population and DFS in all randomized patients with tumor PD-L1 \geq 1%

Secondary endpoints: NUTRFS, DSS, and OS^b

Exploratory endpoints included: DMFS, safety, HRQoL

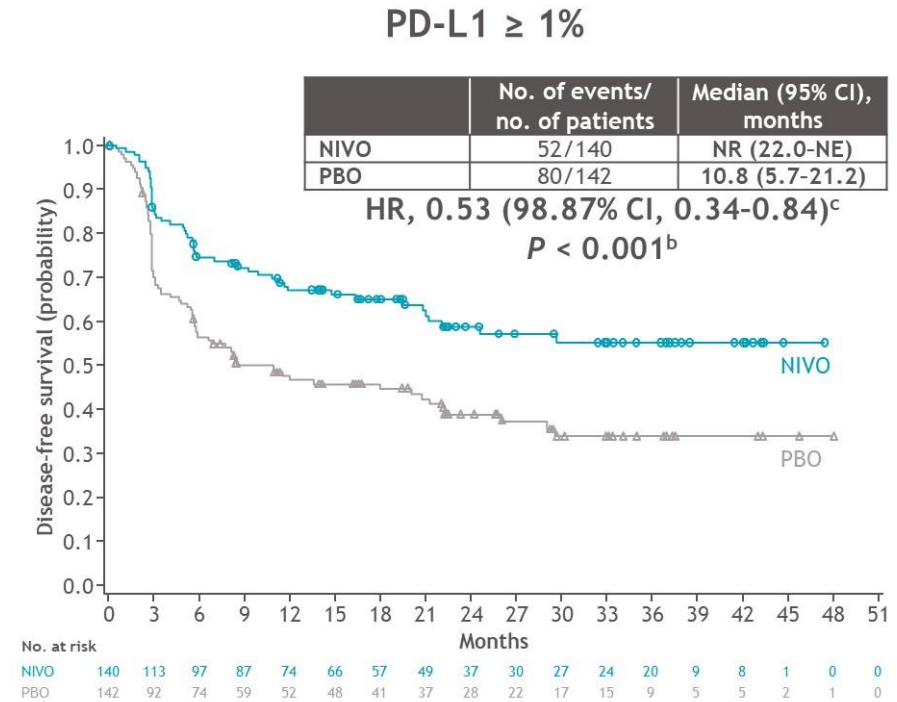
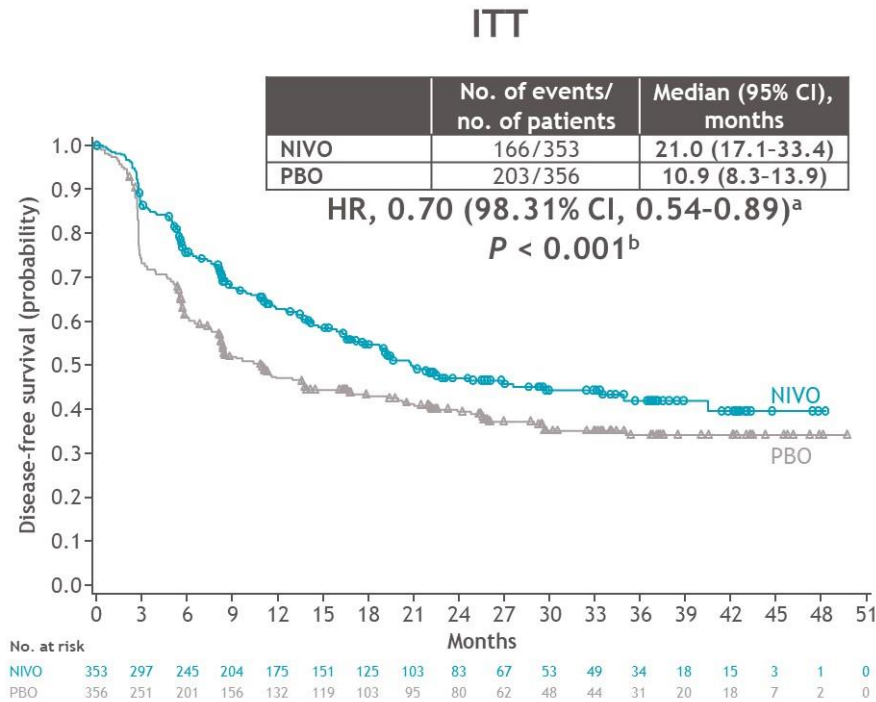
^aDefined by the percent of positive tumor cell membrane staining in a minimum of 100 evaluable tumor cells using the PD-L1 IHC 28-8 PharmDx immunohistochemistry assay.

^bOS data were not mature at the time of the first planned interim analysis. OS and DSS data are not presented.

DFS, disease-free survival; DMFS, distant metastasis-free survival; DSS, disease-specific survival; HRQoL, health-related quality of life; IHC, immunohistochemistry; ITT, intent-to-treat; NUTRFS, non-urothelial tract recurrence-free survival; OS, overall survival; PD-L1, programmed death ligand 1; Q2W, every 2 weeks; R, randomized.



Disease-free survival



Minimum follow-up, 5.9 months.

DFS was defined as the time between the date of randomization and the date of first recurrence (local urothelial tract, local non-urothelial tract or distant) or death.

^aHR, 0.695 (98.31% CI, 0.541-0.894). ^bBased on a 2-sided stratified logrank test. ^cHR, 0.535 (98.87% CI, 0.340-0.842).

CI, confidence interval; NE, not estimable; NR, not reached.



NCCN Clinical Practice Guidelines in Oncology - Bladder Cancer, February 9, 2023

ADJUVANT TREATMENT

Following
cystectomy

- Based on pathologic risk,
 - ▶ If no cisplatin neoadjuvant treatment given and pT3, pT4a, or pN+
 - ◊ Adjuvant cisplatin-based chemotherapy should be discussed (preferred)^y or
 - ◊ Consider adjuvant nivolumab ^{y,cc}
 - or
 - ▶ If cisplatin neoadjuvant chemotherapy given and ypT2–ypT4a or ypN+, consider nivolumab ^{y,cc}
 - or
 - ▶ Consider adjuvant RT in selected patients (pT3–4, positive nodes/margins at the time of surgery)^{aa} (category 2B)

See
Follow-up
(BL-E)

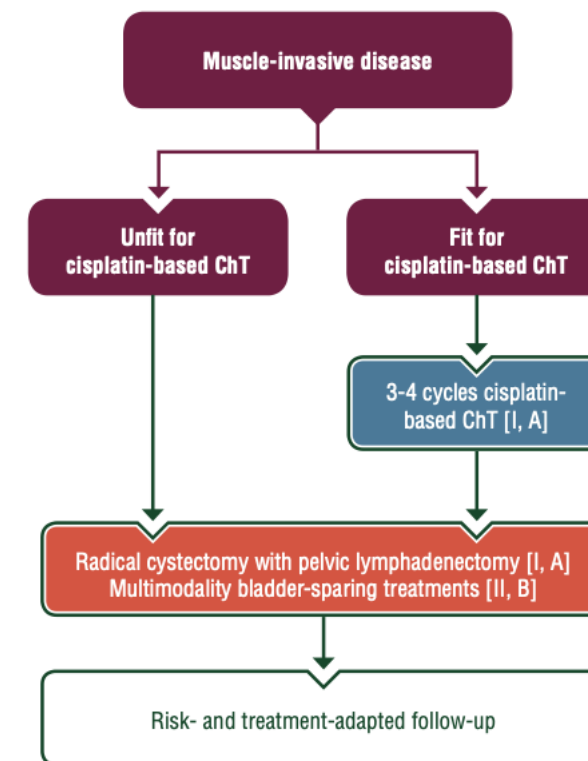
EMA Recommends Extension of Therapeutic Indications for Nivolumab

New indications concern the treatment of unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma and the adjuvant treatment of muscle invasive urothelial carcinoma

Date: 07 Mar 2022

Topics: Immunotherapy; Oesophageal Cancer; Urothelial Cancers

Opdivo as monotherapy is indicated for the adjuvant treatment of adults with muscle invasive urothelial carcinoma (MIUC) with tumour cell PD-L1 expression $\geq 1\%$, who are at high risk of recurrence after undergoing radical resection of MIUC.





JUL 2013

NO EVIDENCE OF DISEASE

DFS ~ 6 years

OCT 2019

Acute pyelonephritis with hematuria

- CT scan: Nodular lesion (50mm x 58mm) in the left renal pelvis with densification of surrounding fat and hilar lymph nodes (~24mm).
- Positive UCy**

★ **Multidisciplinary tumour board NOV 2019:**

- Late recurrence VS primary UTUC stage IV
- Fit for cisplatin
 - > First-line systemic therapy - CDDP/GEM 4-6 cycles



NOV 2019

1st line treatment - CDDP/GEM 6 cycles

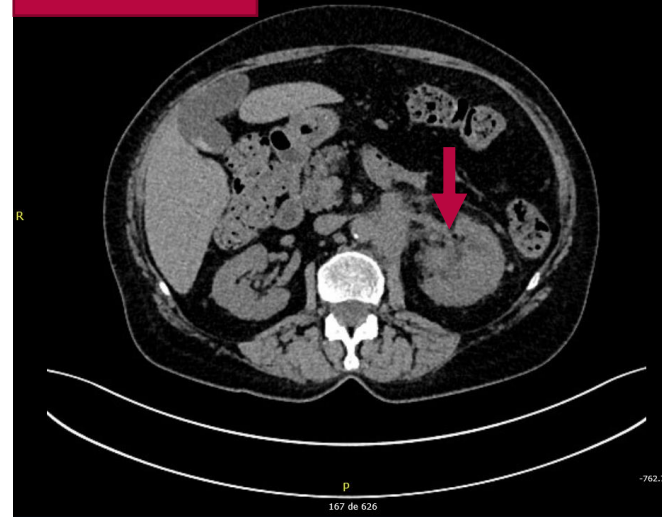
MAY 2020

CT: partial response

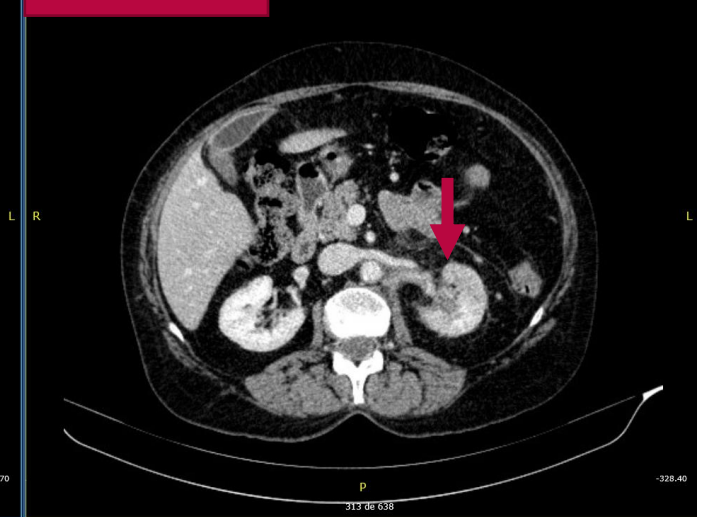
ADVERSE EVENTS:

- Fatigue G1
- PN G2

NOV 2019



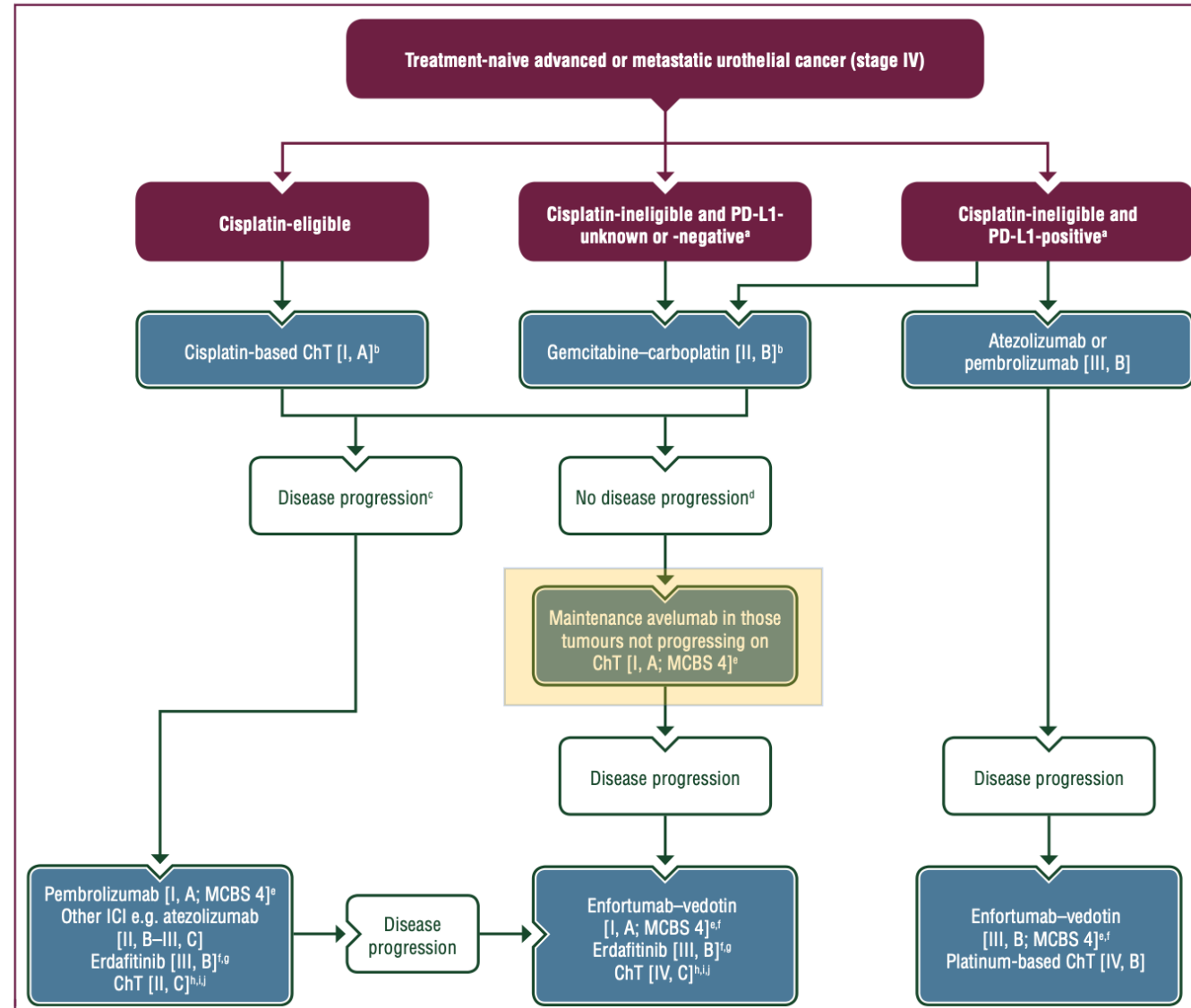
MAY 2020



Multidisciplinary tumour board JUN 2020: Surveillance



2023?





DEC 2020

Disease progression

★ **Multidisciplinary tumour board: 2nd-line treatment – pembrolizumab**

2 years of SD

ADVERSE EVENTS:

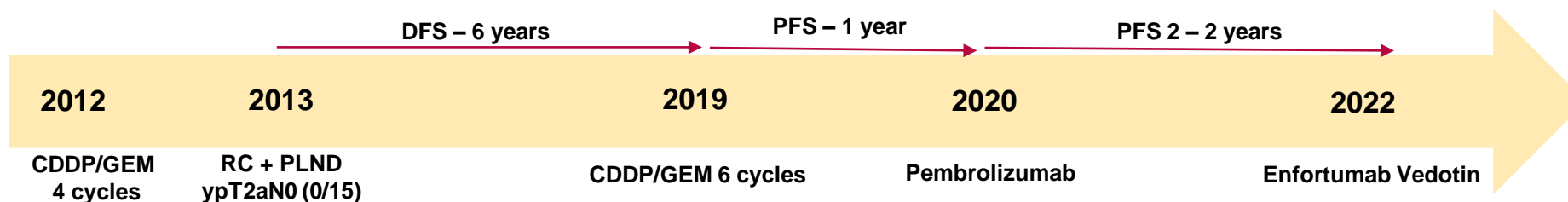
Fatigue G1

Colitis G2

DEC 2022

Disease progression

★ **Multidisciplinary tumour board: 3rd-line treatment – enfortumab vedotin**





CONCLUSIONS

- ❑ Late recurrence of bladder cancer following RC
 - 3.9-12.2% of patients
 - UTUCs are the most common sites of late recurrence
 - Probably associated with an improvement in post-recurrence survival and more favorable clinicopathologic characteristic

- ❑ What is the benefit of adjuvant IT?

- ❑ 2-year of SD on second-line treatment with pembrolizumab



THANK YOU