Integrating knowledge and clinical practice: clinical vignette

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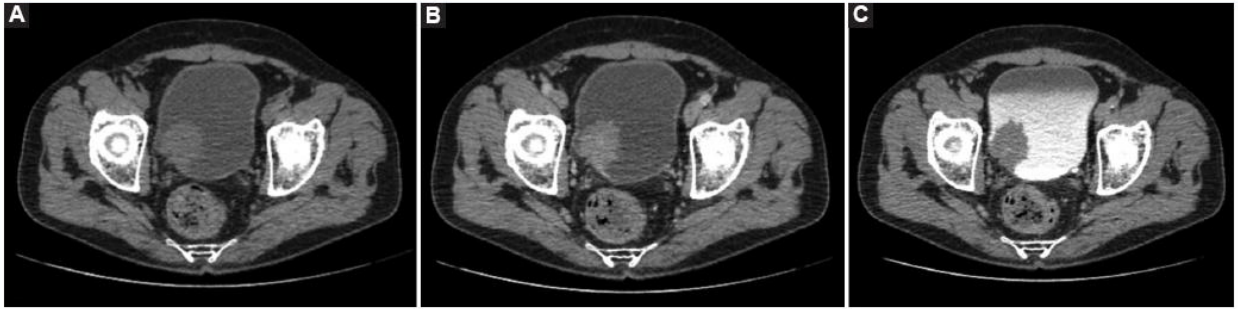
71-year-old male, 17-year former smoker

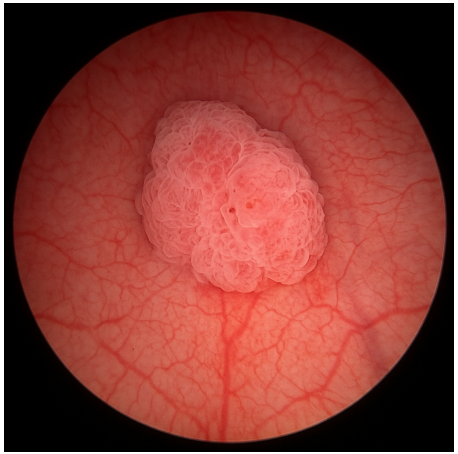
Past medical history of hypertension, intermittent claudication of lower limbs grade 2, dyslipidemia

Treatment: losartan 50 mg, atorvastatin 40 mg, AAS 100 mg

No family history of cancer.

- Presented with gross hematuria in October 2021.
- Baseline CT: 5 cm bladder mass, no lymph nodes or metastases.

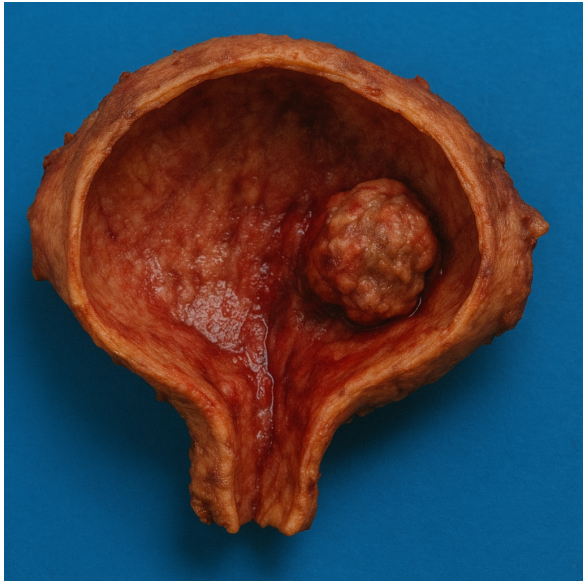




- TURBT: High-grade urothelial carcinoma (cT2) with CIS.
- Biomarkers: PD-L1 CPS 10%.
- Renal function preserved (eligible for cisplatin).

Initial management

- Neoadjuvant cisplatin/ gemcitabine x4 cycles.
- Minimal radiologic response.
- Radical cystectomy + pelvic lymphadenectomy.
- Pathology: ypT3aN1 (2/22 nodes positive), lymphovascular invasion+, negative margins.



Adjuvant treatment

ADJUVANT **NIVOLUMAB** FOR 12 MONTHS DUE TO HIGH-RISK FEATURES.

TOLERABILITY: OVERALL WELL TOLERATED EXCEPT FOR GRADE 1 HYPOTHYROIDISM (MANAGED WITH LEVOTHYROXINE) AND GRADE 1 PRURITUS, BOTH CONTROLLED WITH SUPPORTIVE CARE.

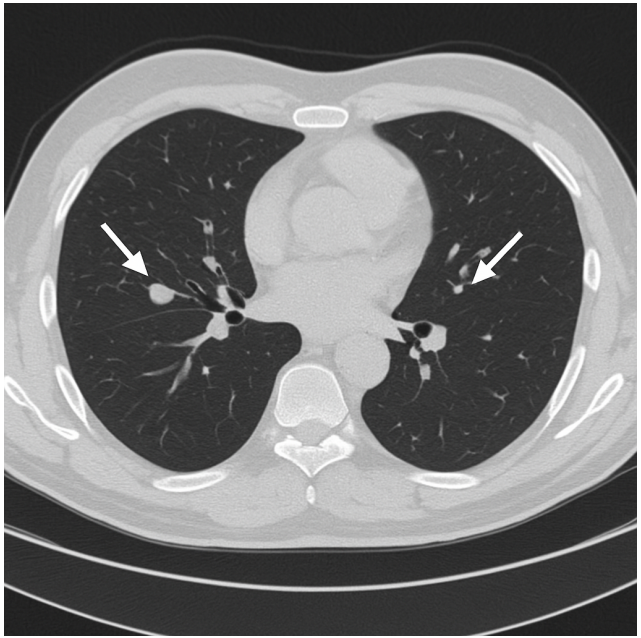
DISEASE-FREE SURVIVAL:

10 MONTHS

AFTER TREATMENT COMPLETION.

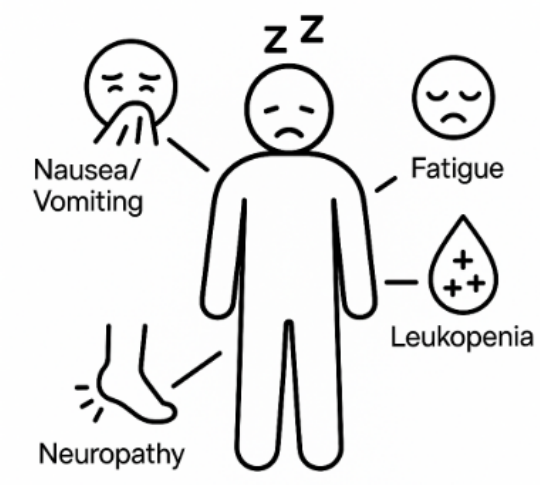
Relapse

- 10 months after completion of nivolumab (February 2024).
- Dry cough and 2 kg weight loss.
- CT: two pulmonary nodules (12 and 17 mm), external iliac lymph nodes (1.4 cm).
- Pulmonar biopsy: metastatic urothelial carcinoma , FGFR3 S249C mutation detected.
- Renal function preserved (eligible for cisplatin).



Therapeutic Sequence Applied

- First-line metastatic: **Cisplatin/ Gemcitabine** rechallenge (interval >24 months since prior platinum). Partial response, progression after 7 months.



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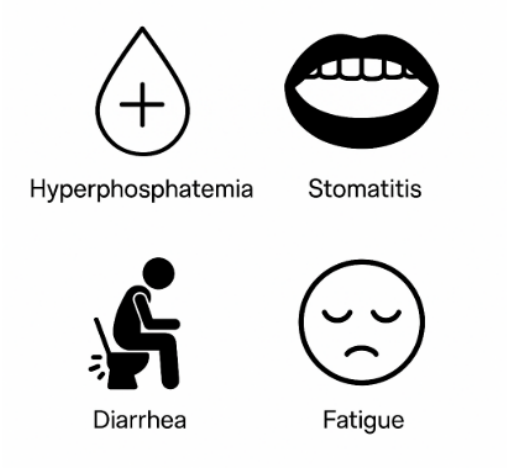
- Second-line: **Erdafitinib** (FGFR3 targeted). Stable disease for 8 months, then pulmonary progression.



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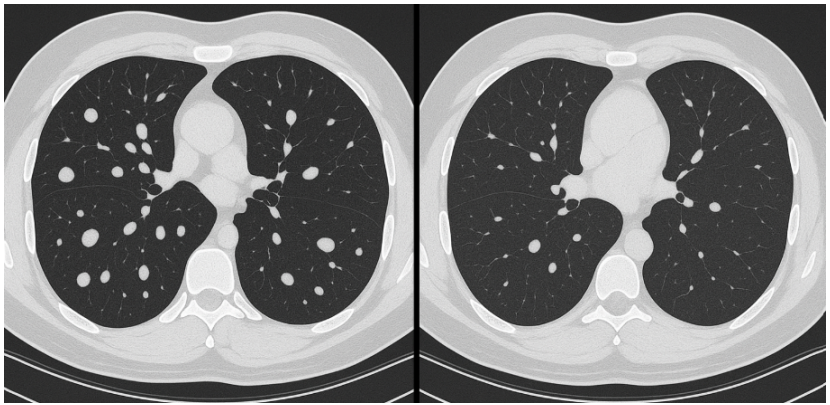
- Second-line: Erdafitinib (FGFR3 targeted). Stable disease for 8 months, then pulmonary progression.
- Third-line: **Enfortumab vedotin** with excellent radiologic and clinical response after 5 months of treatment.
  - ❑After 4 cycles, grade 2 neuropathy requiring dose reduction.



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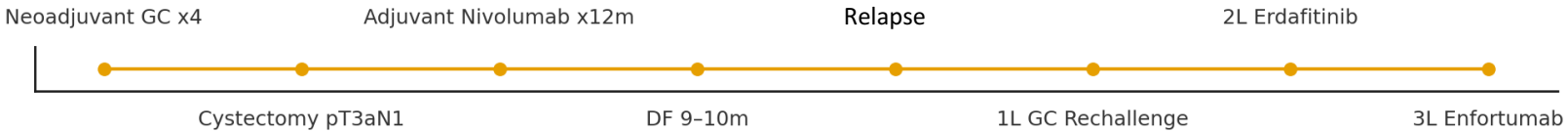

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UNANSWERED QUESTIONS

- What is going to be the role of CPI in the perioperative setting?
  - ADJUVANT? PERIOP w/ chemo? PERIOP w/ ADCs?
- How does CPI in the periop setting affects the efficacy of CPI based combos [i.e. EV PEMBRO]?
  - Nobody pre treated with periop CPI should be treated with CPI combos?
  - Is it time dependent?
  - Do we have any biomarker?
- Is chemotherapy rechallenge an option in certain patients?
- In FGFR mutants what treatment option should be prioritized?
- If we had access to 1st line EV+Pembro what would be the treatment of choice upon progression?

LET US SEE IF OUR SPEAKERS CAN RESOLVE THESE QUESTIONS

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