
بسم الله الرحمن الرحیم

Molecular Imaging in Neuroendocrine Differentiation of Prostate Cancer

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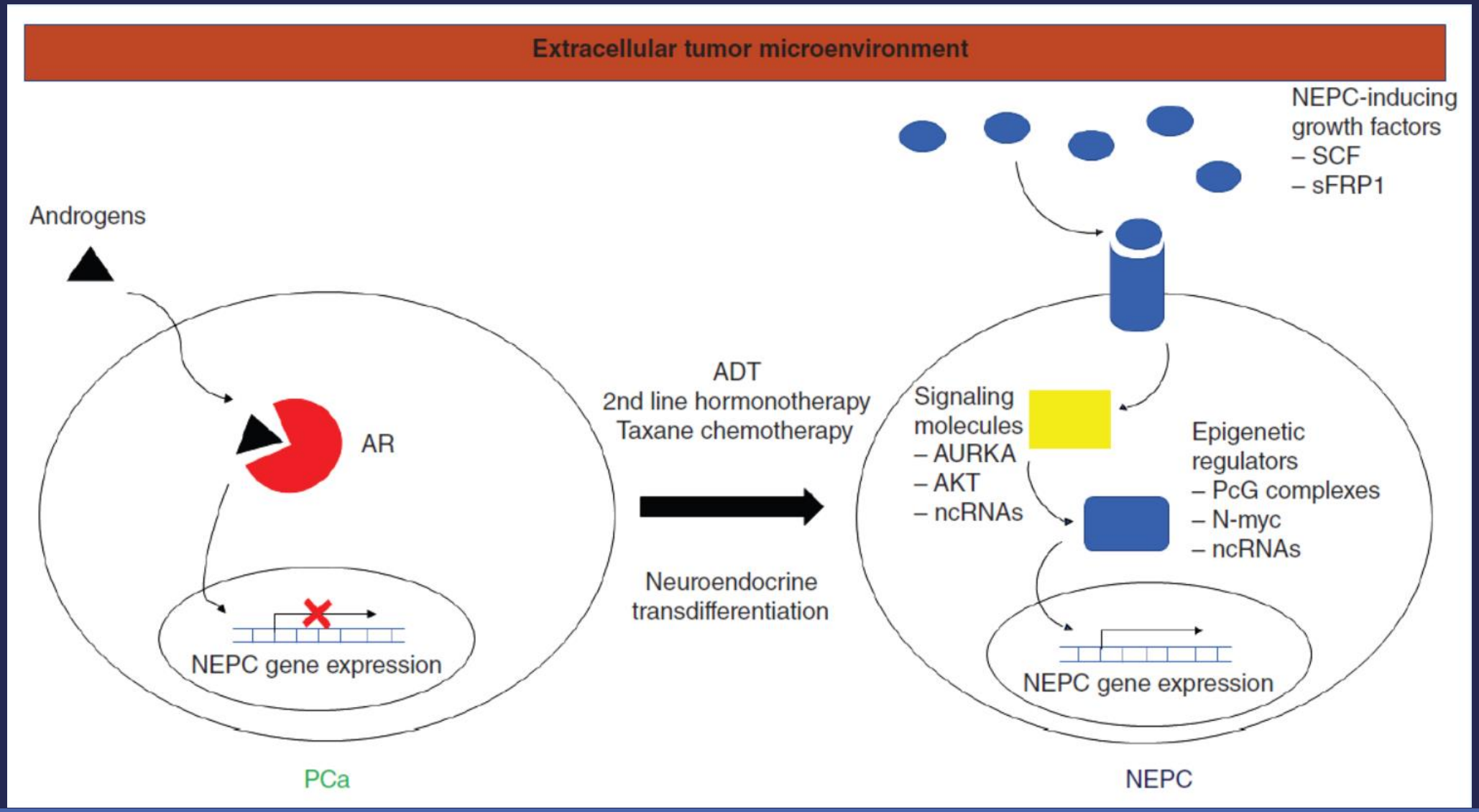
Treatment-emergent Neuroendocrine Prostate Cancer (t-NEPC)

Neuroendocrine Prostate Cancer may arise de novo, but the large majority of cases occur in patients with **CRPC** that have been treated with hormonal therapy and⁄or taxane-based chemotherapy. Clinically, **t-NEPC** is an extremely aggressive malignancy that is resistant to current therapies used in the context of advanced prostate adenocarcinoma.

In addition, **t-NEPC** displays high proliferative rates and tumor dissemination can occur quite rapidly. Unlike **CRPC**, which tends to produce osseous metastases, **t-NEPC** typically disseminates to visceral organs such as lung and liver.

The IHC profile of t-NEPC includes the expression of neuroendocrine markers such as (SYP), (CHGA) and (NSE), as well as absent AR and PSA expression. Once considered a very rare occurrence, t-NEPC has become an increasingly recognized clinical problem. Recent evidence indicates that approximately one out of six patients with progressive hormone-resistant PCa has NEPC. In keeping with this evidence, autopsy studies have shown that neuroendocrine *foci* may be present in about 10–20% of CRPC patients. Given the extensive targeting of AR pathway and testosterone metabolism by recently developed drugs, the incidence of t-NEPC is expected to rise significantly in the near future. Unfortunately, t-NEPC is currently difficult to diagnose because it often arises in patients with multiple metastases, a condition that usually discourages clinicians from performing biopsies. As a result, the incidence of t-NEPC is usually underestimated and patients with undiagnosed t-NEPC are treated unnecessarily with the same regimen as patients with AR-positive prostate adenocarcinoma, with no success.

Molecular mechanisms involved in neuroendocrine prostate cancer pathogenesis



Screening & diagnosis

- ✓ Imaging
- ✓ Serum markers
- ✓ Biopsy of metastatic tissues

In particular, rapidly progressing lesions without a proportional PSA rise, in patients exposed to hormonal therapies should prompt BX.
BX should also be considered in CRPC patients with visceral metastases or NEPC-associated paraneoplastic syndromes.
Finally, clinicians should consider BX in the context of elevated serum markers such as CHGA and NSE.

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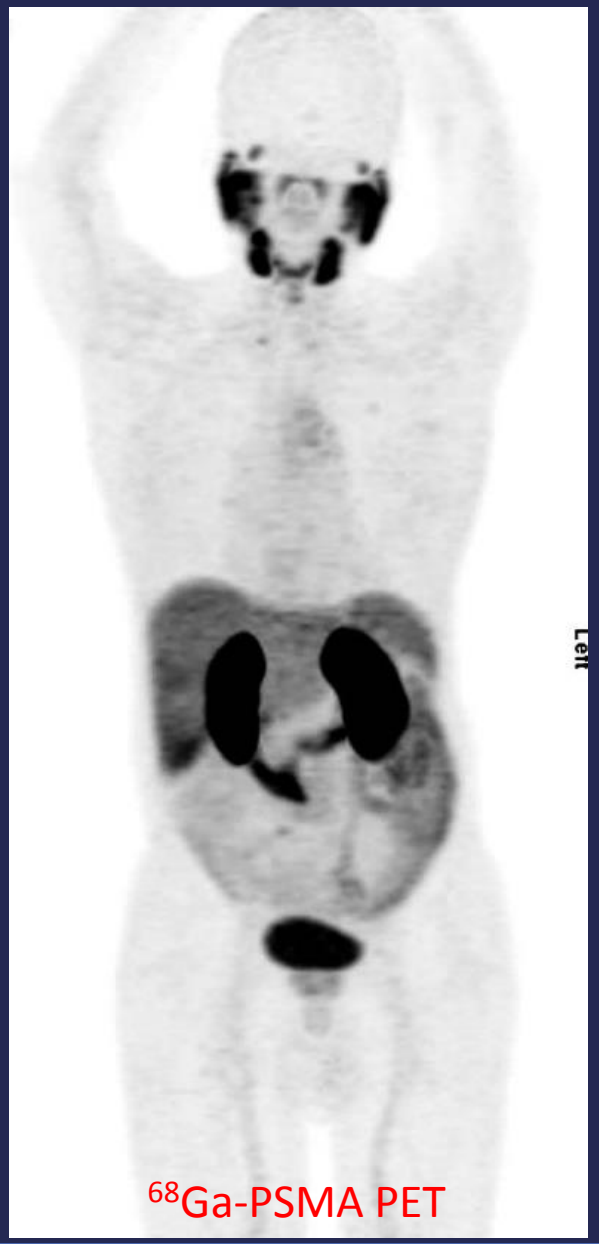
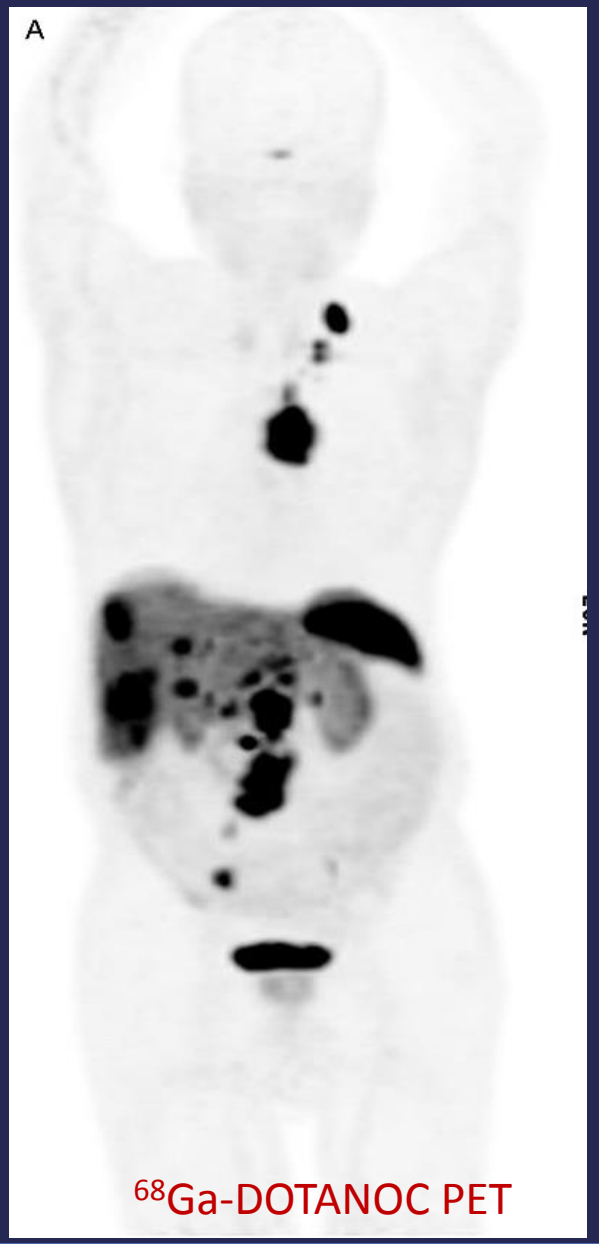
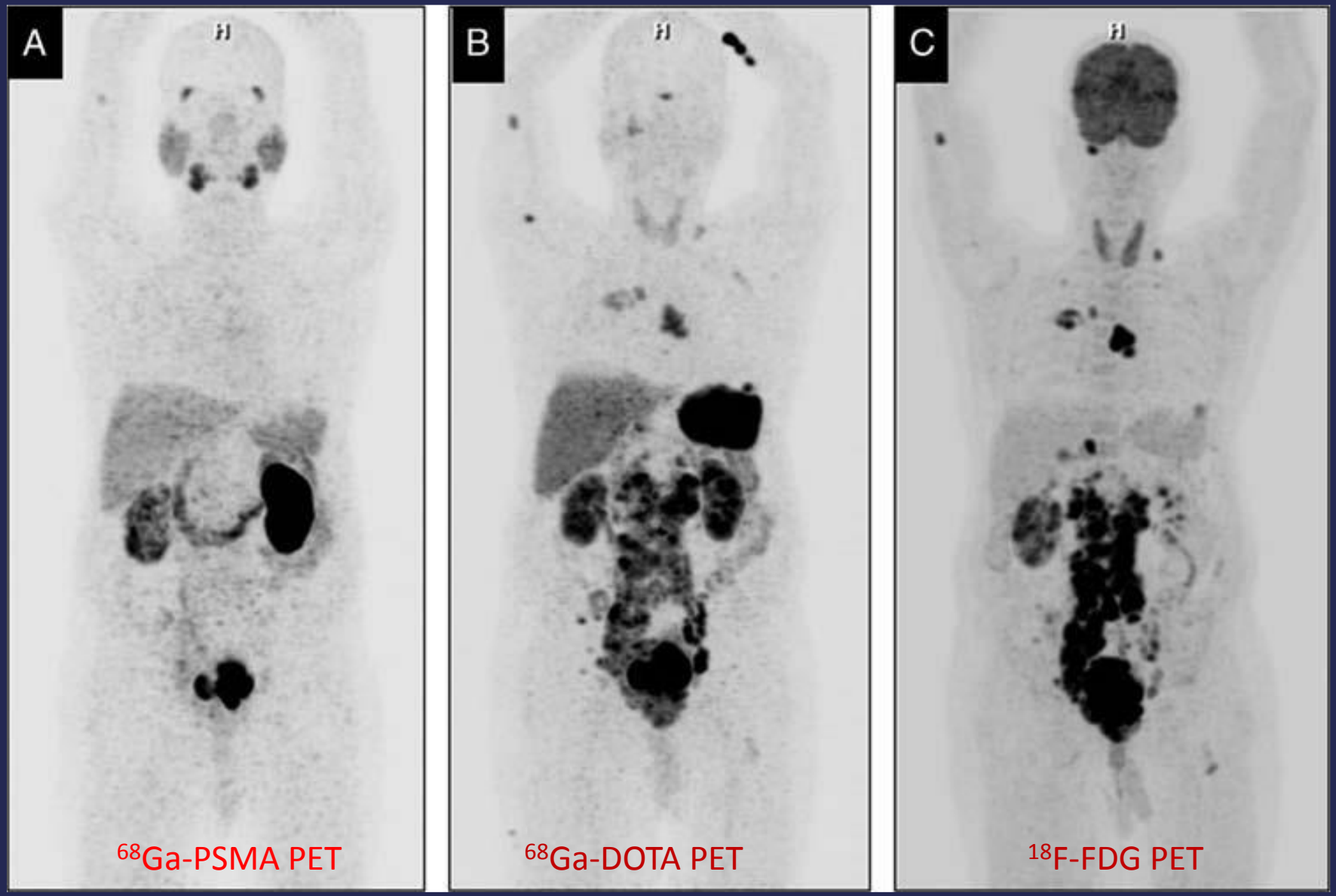
- ^{68}Ga-PSMA PET/CT
- ^{18}F-FDG PET/CT
- ^{68}Ga-SSTR PET/CT (DOTATATE, DOTANOC, DOTATAOC)

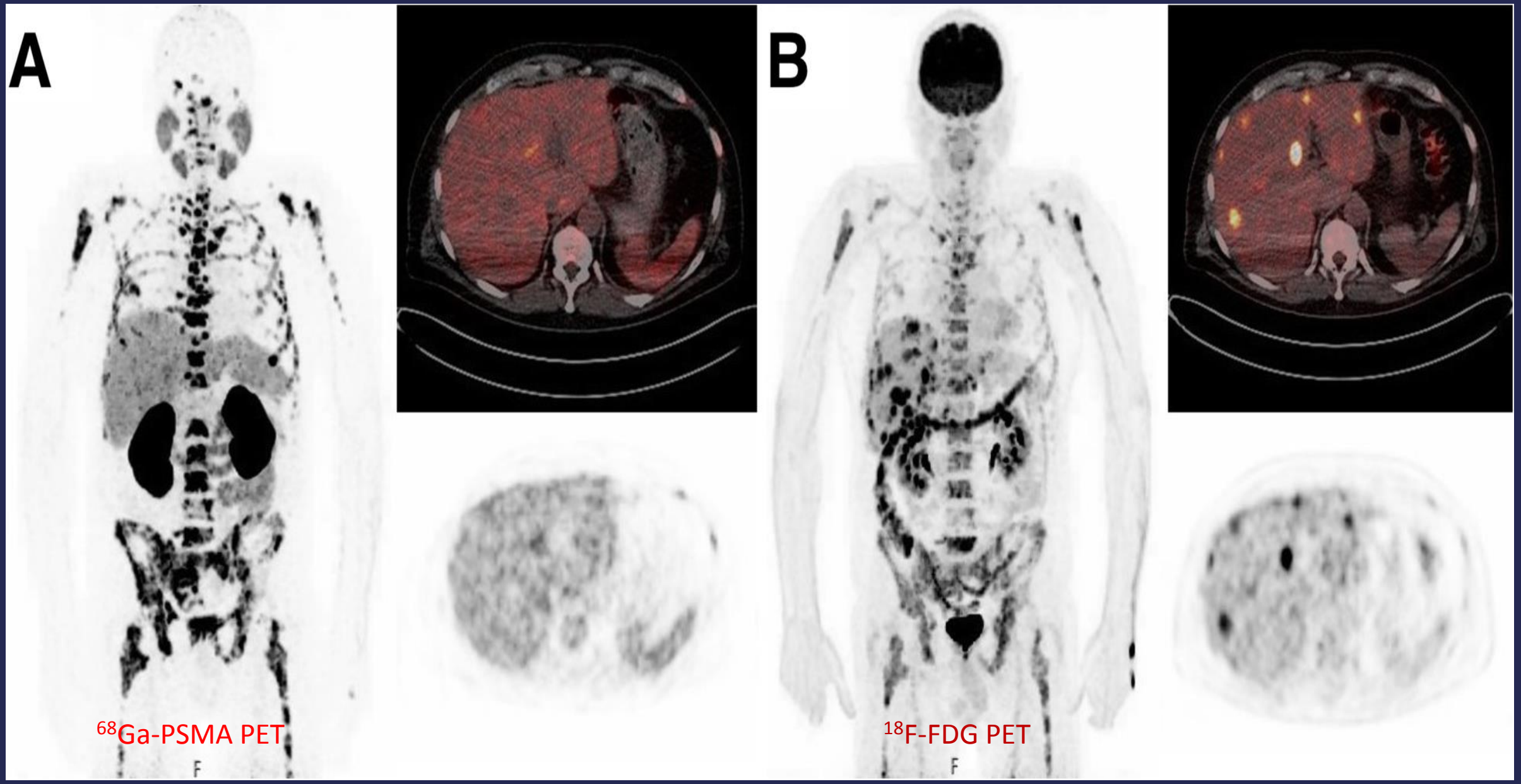


^{68}Ga-PSMA PET



^{68}Ga-DOTANOC PET


A
B
C
^{68}Ga-PSMA PET
^{68}Ga-DOTA PET
^{18}F-FDG PET


A
B
^{68}Ga-PSMA PET
^{18}F-FDG PET

Future perspective & research topics for t-NEPC

- Appropriate diagnostic algorithm
- Efficient prevention
- Effective therapy


✓ We all hope we can cure all cancers one day …