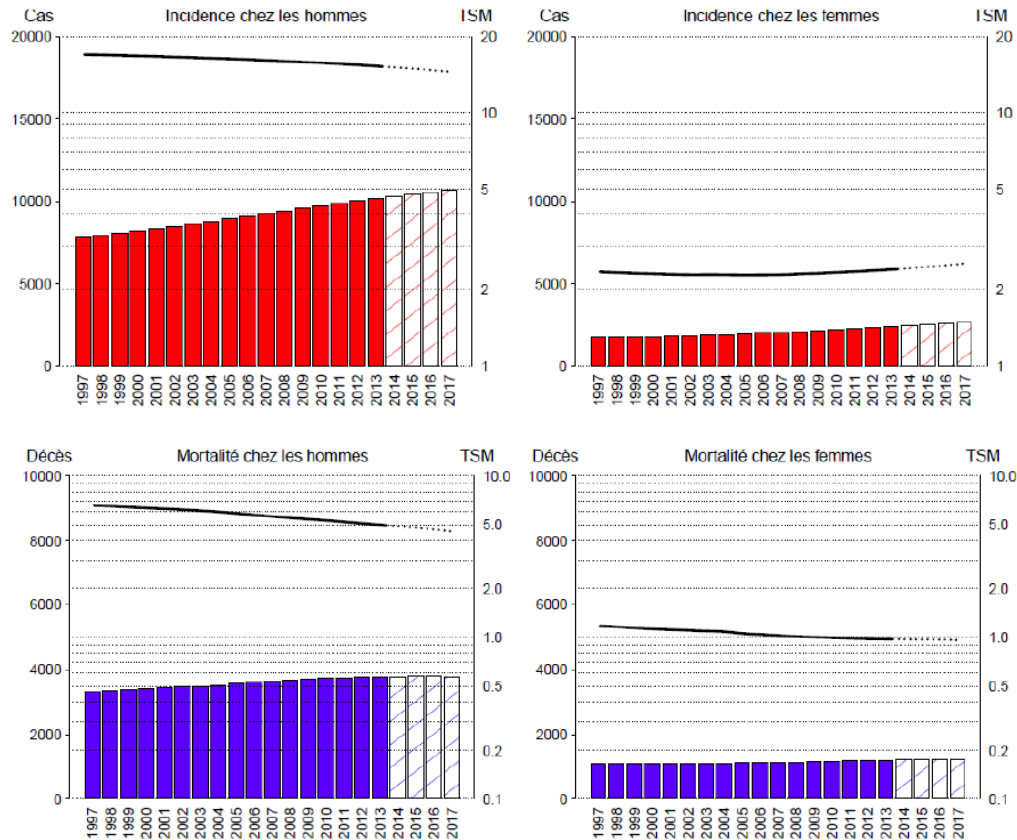


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Loriot Yohann, Département de médecine & INSERM U981
Gustave Roussy, Cancer Campus, Grand Paris



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L'incidence des cancers urothéliaux augmente et la mortalité ne se réduit pas

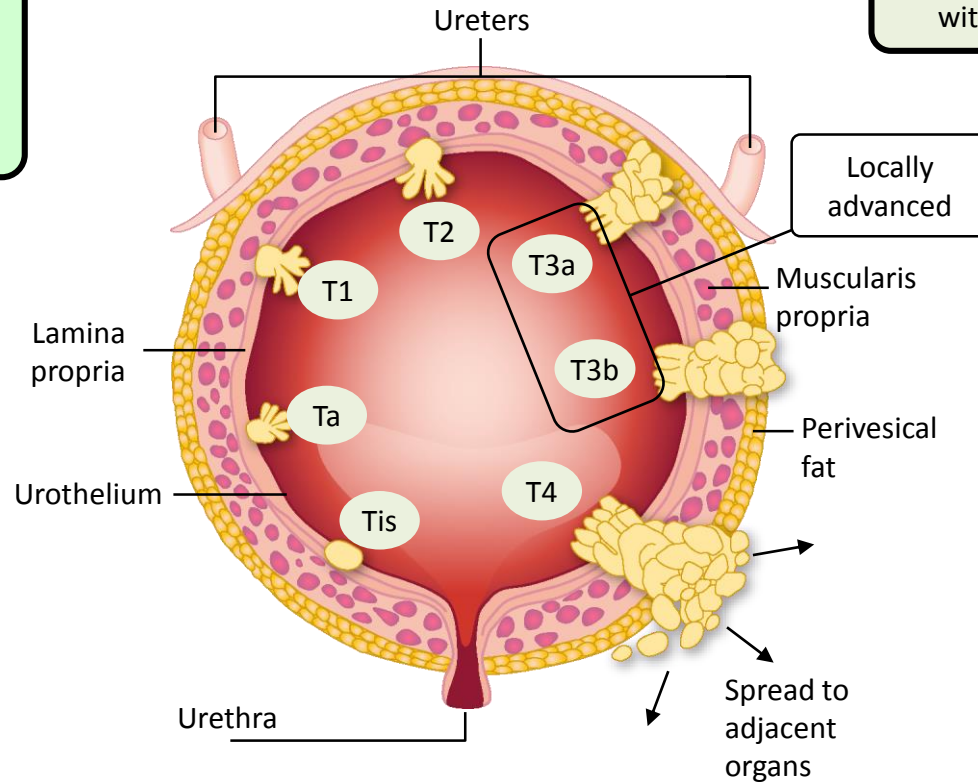
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Non-muscle-invasive bladder cancer (NMIBC)

(Tis, Ta, T1)
≈51–75% of patients diagnosed when tumour is non-invasive¹⁻⁴

Muscle-invasive bladder cancer (MIBC)

(T2, T3a, T3b)
≈30–42% of patients diagnosed with organ-confined MIBC^{1,4}



Metastatic disease (T4)

≈4% of patients diagnosed at metastatic stage^{1,5}

Les formes d'emblée métastatiques sont rares

Agir tôt est l'une des approches nécessaires pour réduire la mortalité

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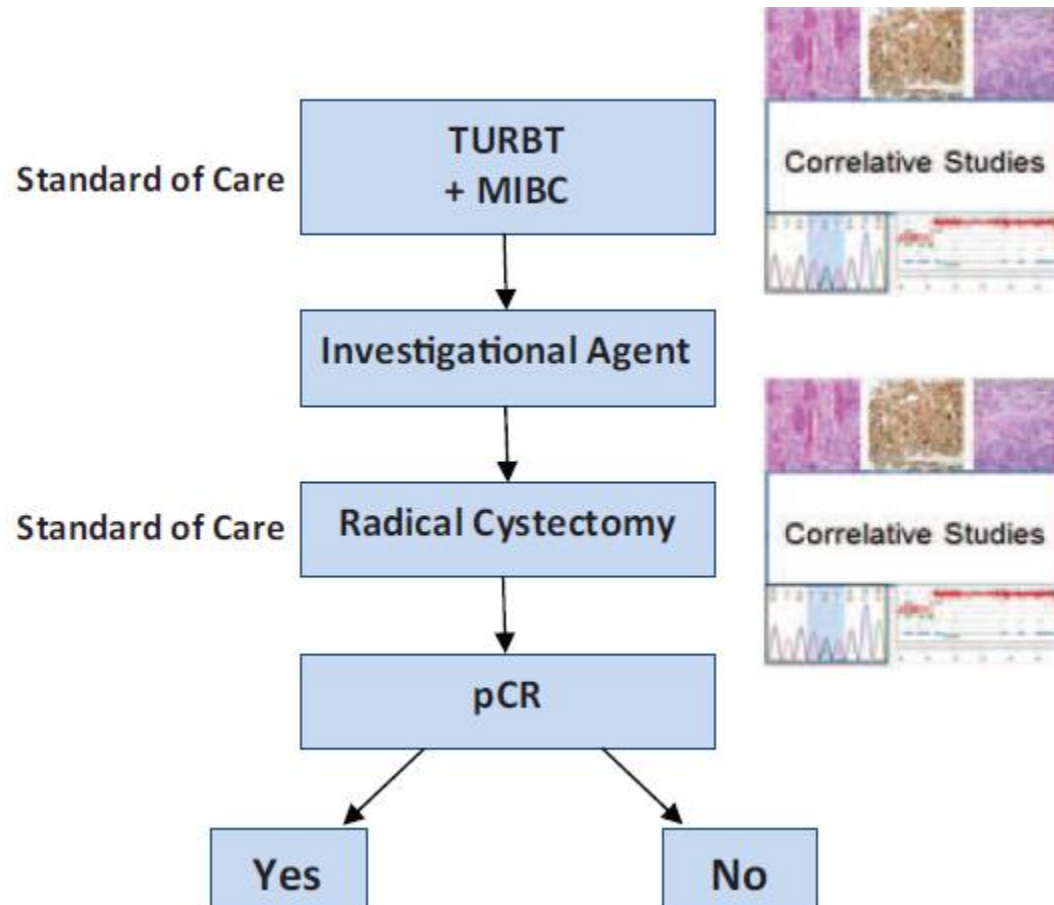
Recommendations	Strength rating
Offer neoadjuvant chemotherapy (NAC) for T2-T4a, cN0M0 bladder cancer. In this case, always use cisplatin-based combination therapy.	Strong
Do not offer NAC to patients who are ineligible for cisplatin-based combination chemotherapy.	Strong

30-40% des patients sont inéligibles au cisplatine

Objectifs du groupe tumeur urothélial

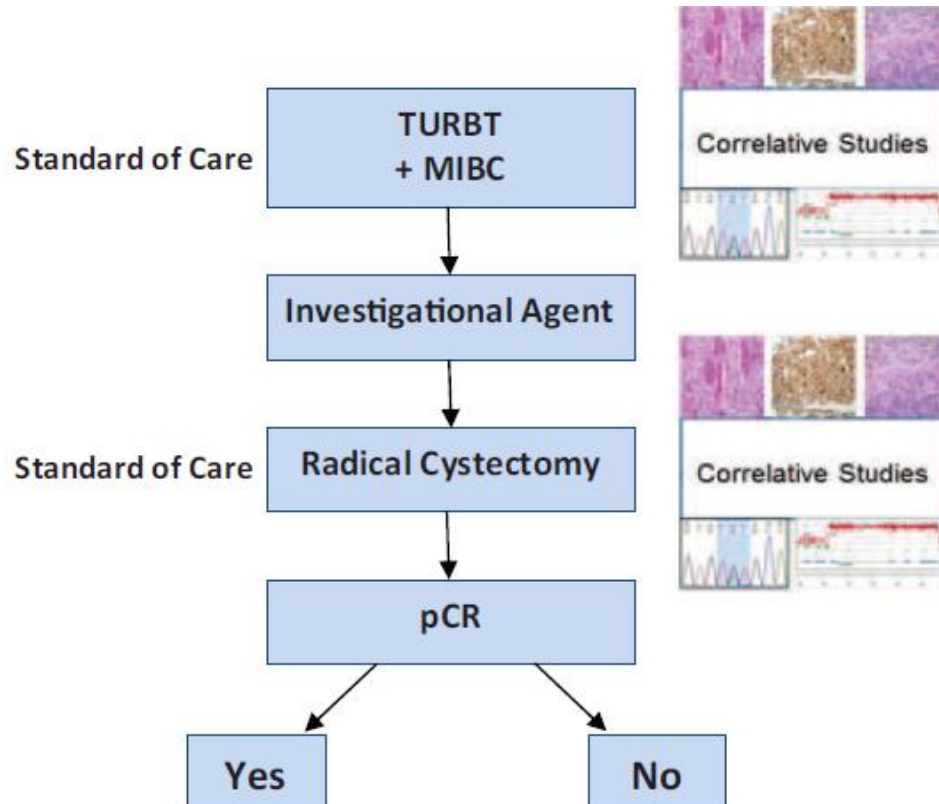
- continuer de promouvoir quelques études de phase 3
- S'intéresser aux stades les plus précoces (TVNIM) ;
- Développer une expertise de recherche dans les tumeurs rares ;
- Proposer des études avec des méthodologies originales et adaptant les nouvelles technologies.

Neoadjuvant setting to be used for drug development



Even though pT0 is not a true surrogate endpoint for OS, pCR can be used for accelerated drug development

PANDORE : objectifs

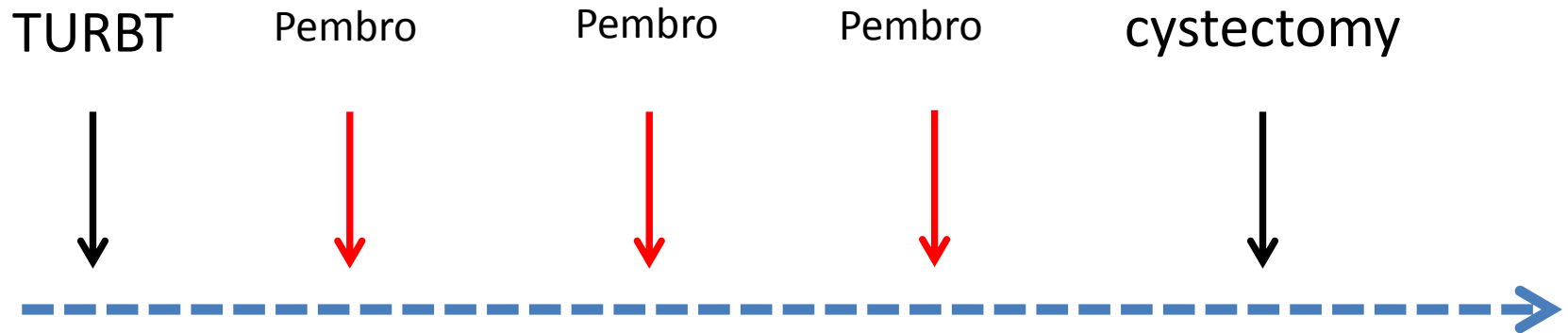


Objectif médical: apporter une proposition d'amélioration de prise en charge dans une population de patients graves

Objectif scientifique: comprendre des mécanismes d'action et de résistance à de nouvelles thérapies

PANDORE-1 STUDY

Hypothesis: checkpoint inhibitors activate CD8 T Cells leading to antitumor activity in neoadjuvant setting

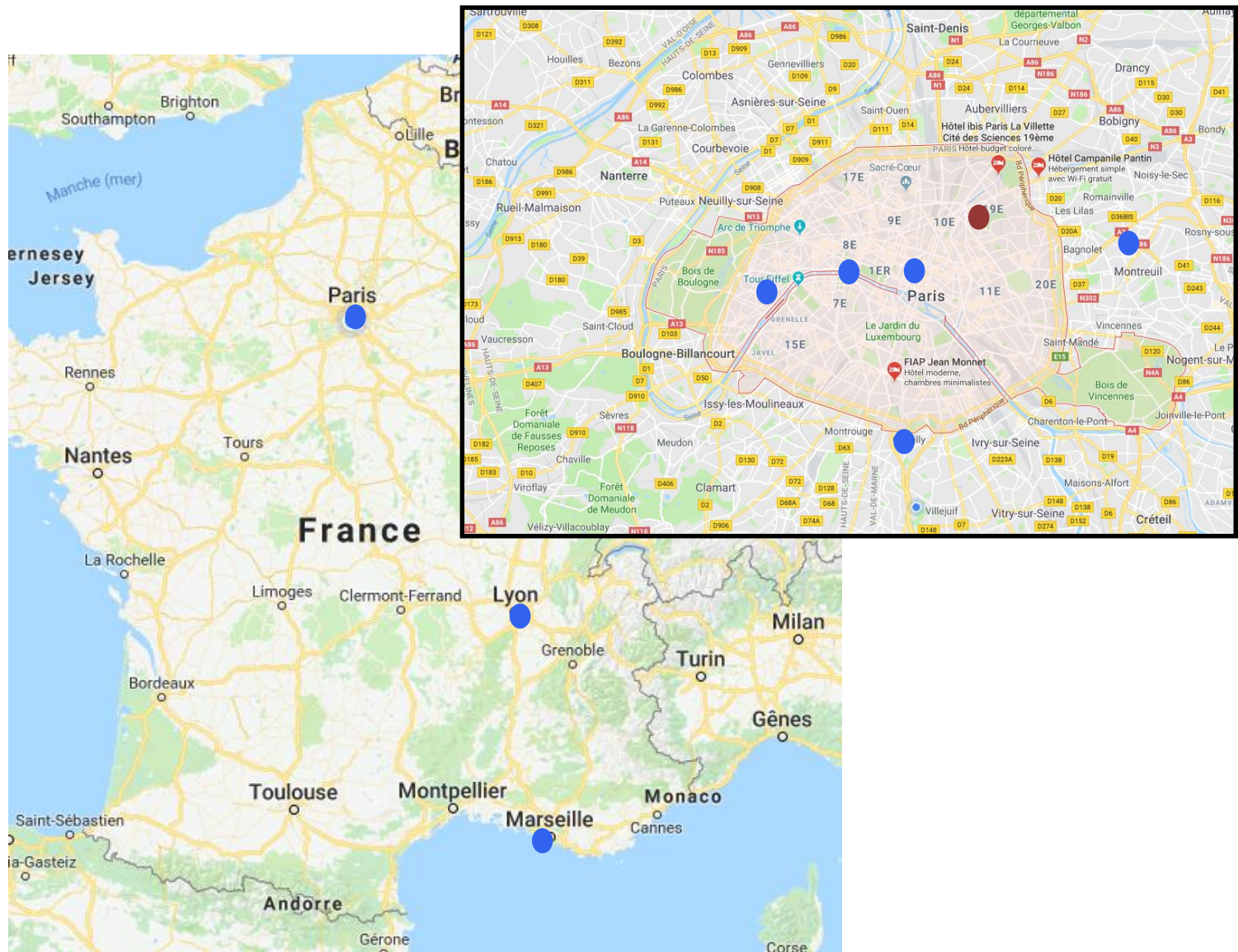


Primary endpoint: pathological response rate

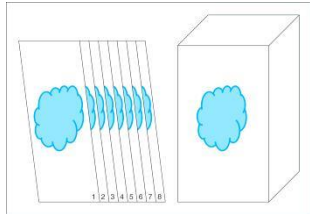
Secondary endpoint: safety

Translational studies: IHC / immunomonitoring / RNA seq /WES

PANDORE STUDY



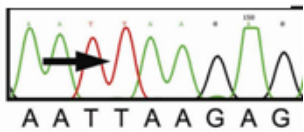
How PD1 works and why TC may resist ?



IHC multiplexing

Immune cell populations

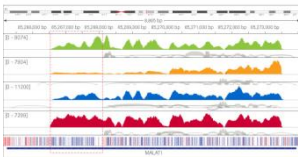
Yves Allory, Institut Curie



WES
TCR seq

Clonal evolution
Neoantigen analysis

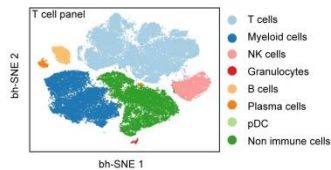
U981, GR



RNA seq

DEG, immune cell population

U981, GR



cytof

immune cell population

U1015, GR



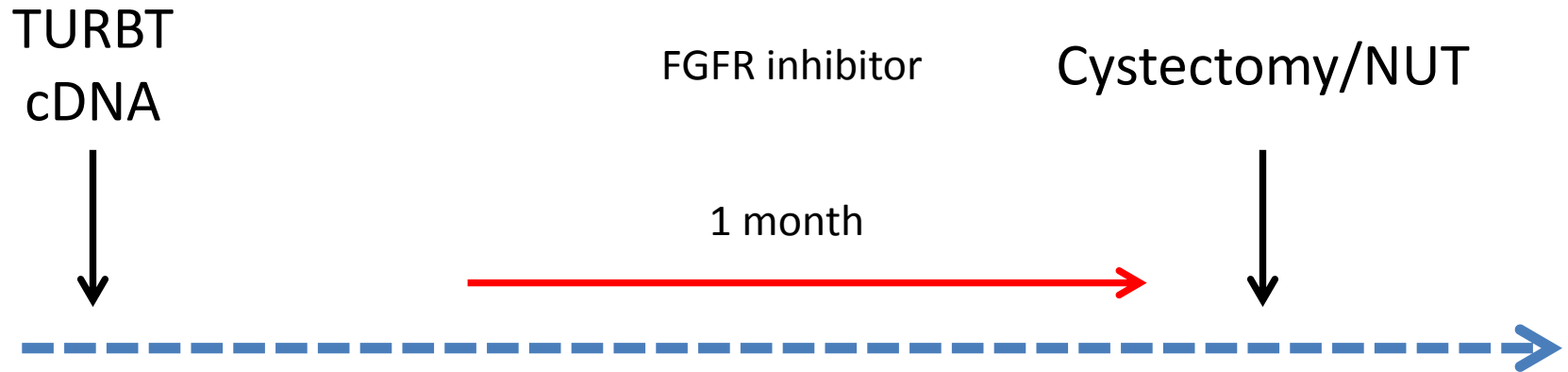
cDNA

Clonal cell population

U981, GR

PANDORE-2 STUDY

Hypothesis: early oncogene-deaddiction leads to antitumor activity in neoadjuvant setting



Primary endpoint: pathological response rate in FGFR2/3 altered MIBC / UTUC

Secondary endpoint: safety

Translational studies: IHC / immunomonitoring / RNA seq /WES