Personalized medicine

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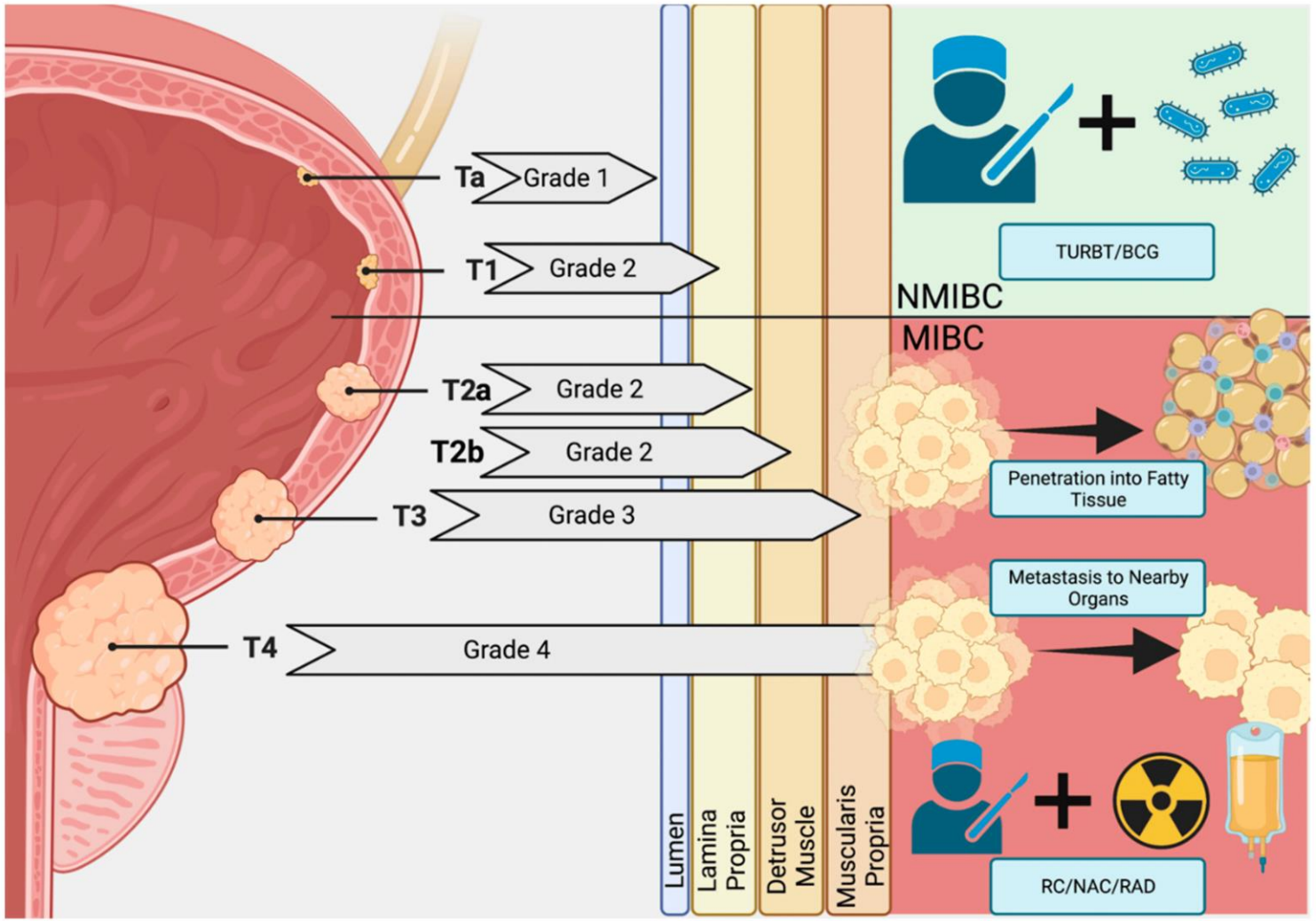
SAMEN GRENZEN VERLEGGEN

Conflict of interest

None

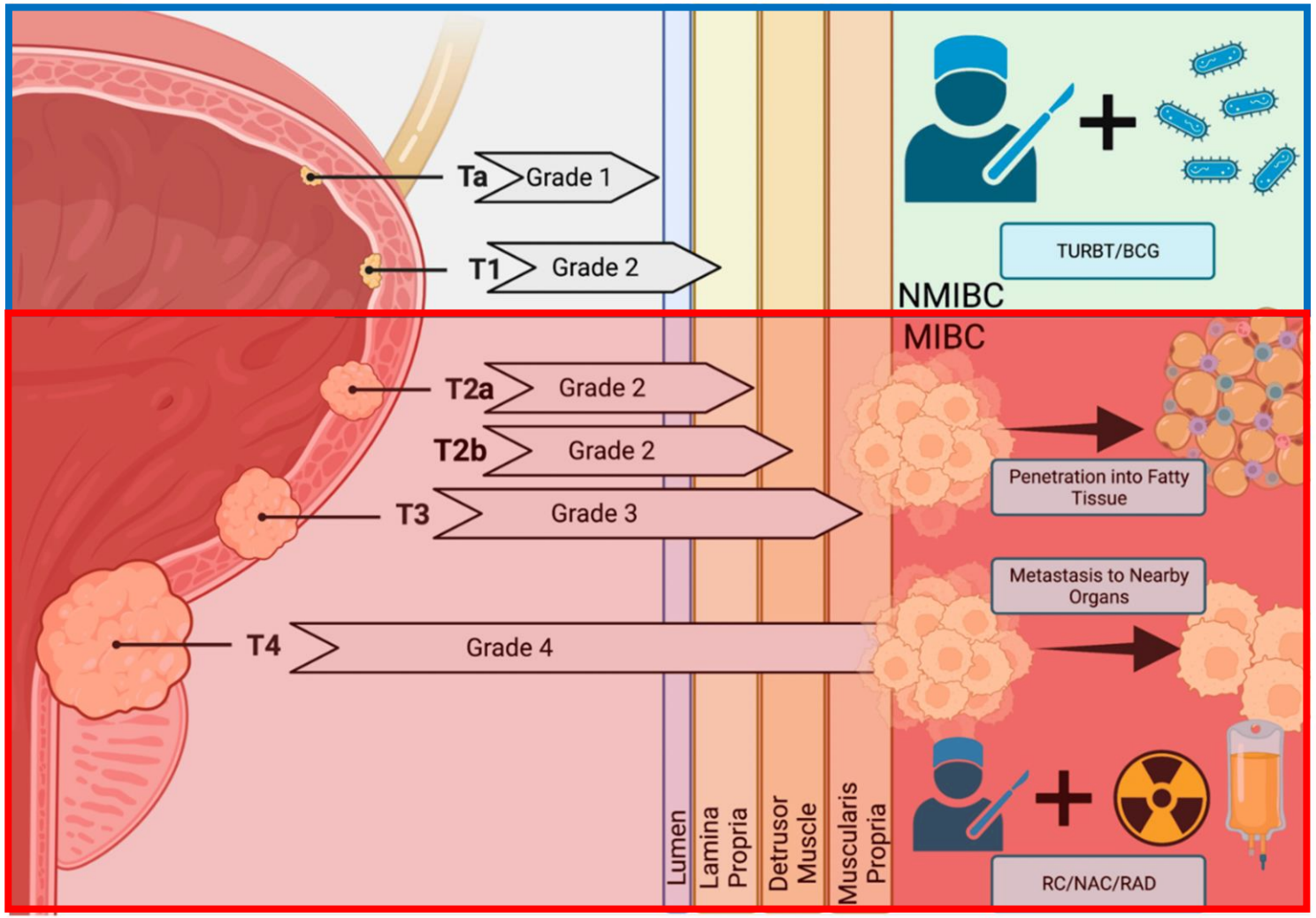
Bladder cancer infographic



Biomedicines 2023, 11(2), 539; https://doi.org/10.3390/biomedicines11020539

Bladder cancer infographic

70% NMIBC



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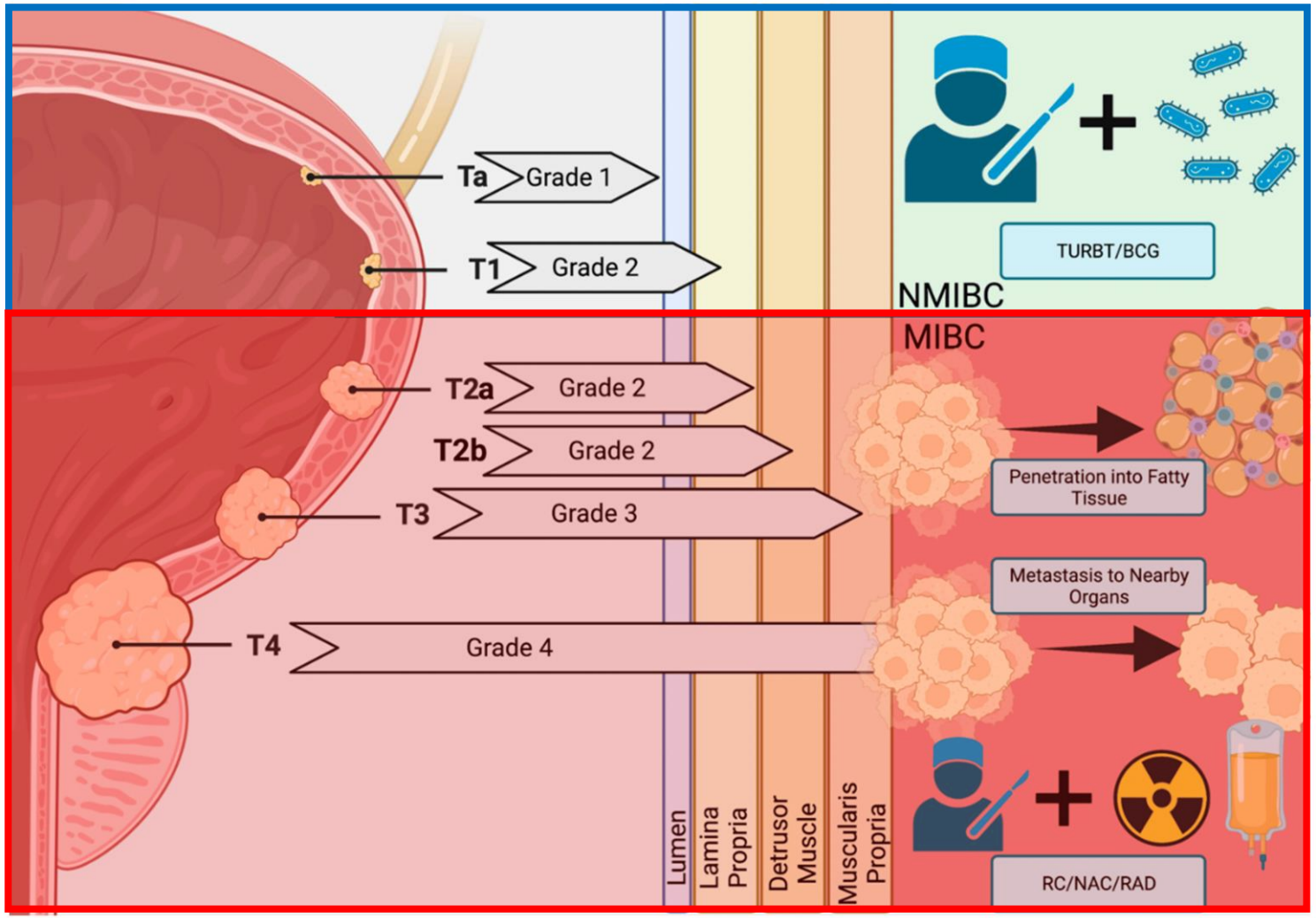
Bladder cancer infographic

70% NMIBC

Recurrence



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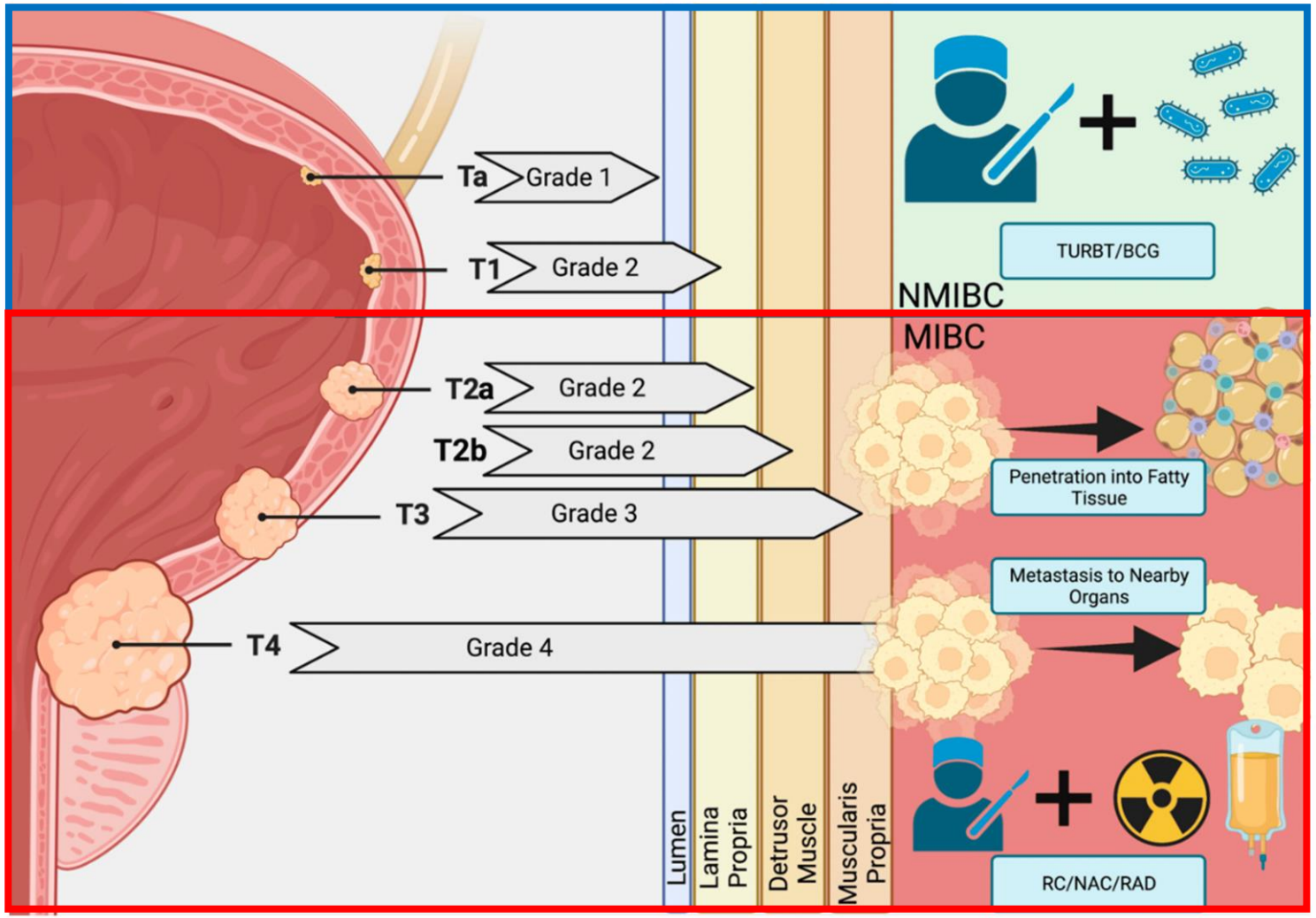
Bladder cancer infographic

70% NMIBC

Recurrence

Progression



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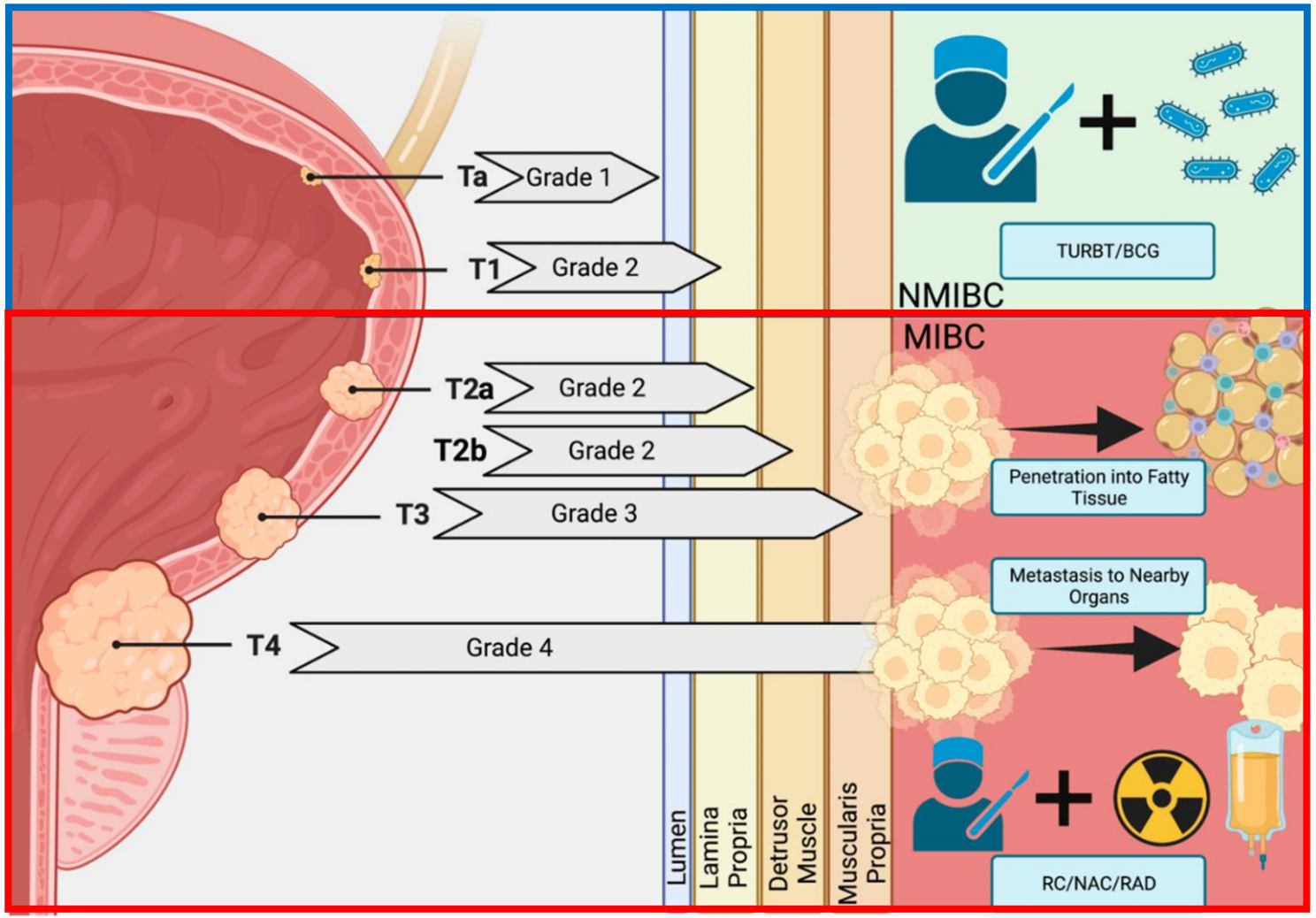
Bladder cancer infographic

70% NMIBC

Recurrence

Progression

Lethal disease



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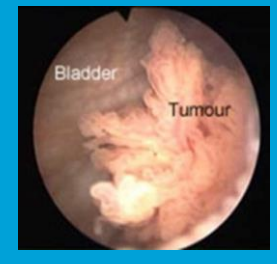
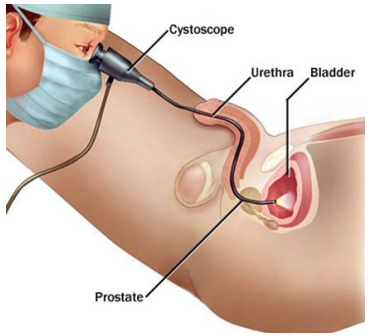
NMIBC – longitudinal patient journey

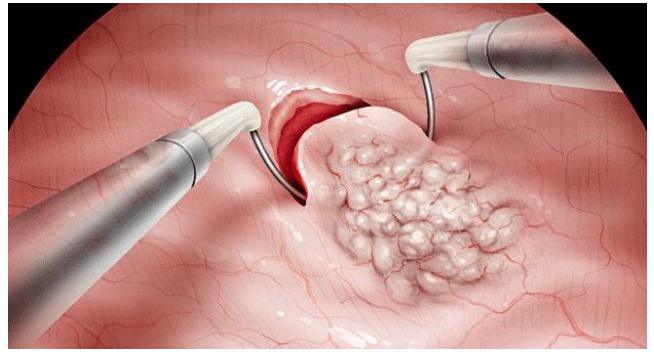


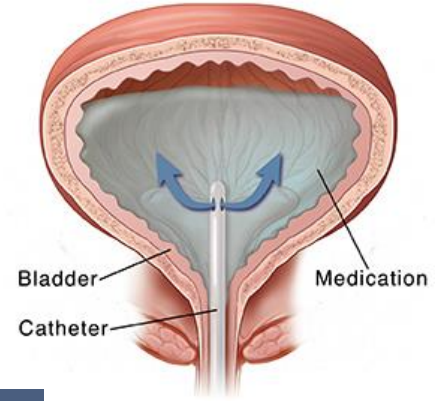
Recurrent cystoscopies

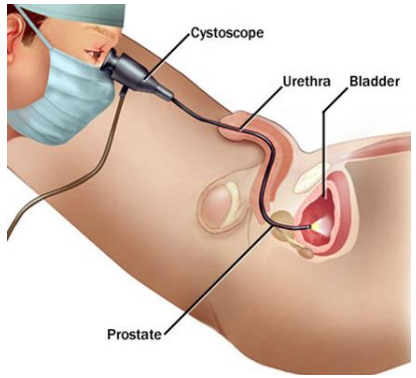
Recurrent TURBT procedures

Bladder instillations









Progression

Cystectomy

Chemotherapy

(N)MIBC - ATHENA

Prevalent – omnipresent in urological practices

Bothersome due to many interventions (recurrence)

Expensive due to many interventions (recurrence and progression)

Potentially *dangerous* (progression)

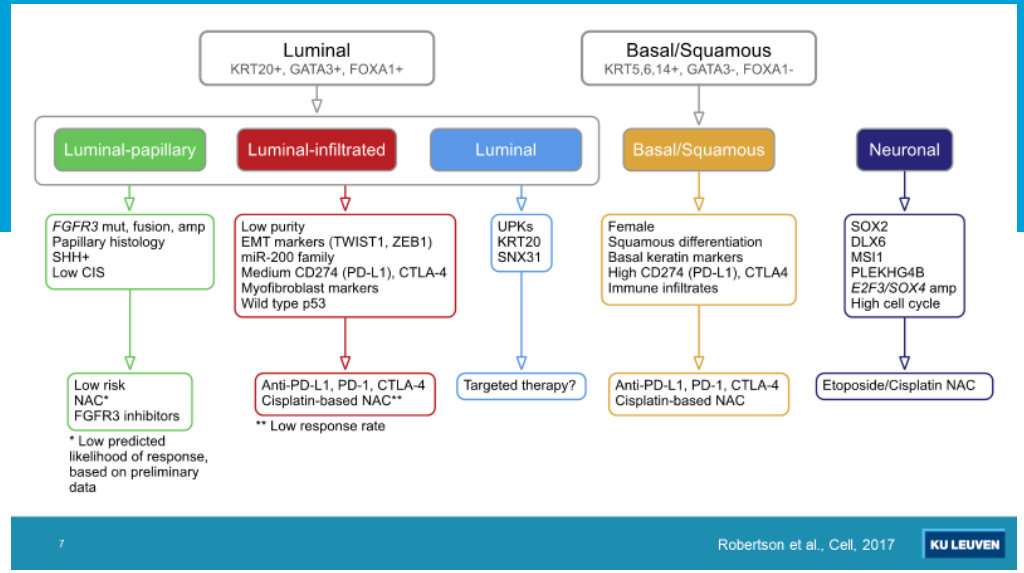
Bothersome due to potentially dangerous (progression)

Typically a disease with a *longitudinal* trajectory

Notorious for *practice variation* and non-adherence to guidelines

→ Can we consistently extract data from the EHR?
→ Can we visualize these data?

(N)MIBC



OMICS have entered the field

OMIC classification of disease has been proposed (not widely accepted or used in clinical practice)

New medical *disease targets* are currently present

→ Can we incorporate this knowledge in disease management?
→ Can we link this knowledge to current disease risk groups?
→ Can we refine current disease risk groups?

NMIBC – ATHENA- WP1

Standardized data collection in different hospitals

Generation of a data catalogue (EHR → OMOP) in different hospitals

(automated) data extraction→ generic ready to analyse worksheet for multifactorial analysis and machine learning

Visualisation of longitudinal patient journey

Generate OMIC data on a retrospective dataset

Generate OMIC data on a prospective dataset

Scale project for use in multihospital setting

NMIBC – ATHENA – key research questions

Q1: Is there a **difference in transcriptomic profiles** (either by single-cell RNA sequencing or bulk sequencing) between patients

- Patients with low-/intermediate-/high-risk NMIBC/m(-) MIBC/m(+) MIBC at first diagnosis
- Patients with intermediate-/high-risk NMIBC who progress to MIBC
- Patients with BCG-naïve intermediate-/high-risk NMIBC recurrence

Q2:Is there a **difference in transcriptomic profiles** (either by single-cell RNA sequencing or bulk sequencing) between patients

- Patients with intermediate-/high-risk NMIBC recurrence during or after BCG
- Patients with intermediate-/high-risk NMIBC recurrence after anti-PD-1/PD-L1 treatment or nadofaragene firadenovec (Instiladrin®), FGFR inhibitor

NMIBC – ATHENA – key research questions

Q3: What is the **natural history & epidemiology of DNA alterations** (as FGFR or other biomarkers) in bladder cancer (logitudinal from NMIBC – MIBC – mUC)?

- How do they change through the evolution of the disease?
- How will certain treatments effect these changes?

Q4:Can we **predict recurrence/progression timelines & outcomes** in correlation with epigenetic/transcriptomic biomarkers & clinical/pathological data for intermediate-/high-risk NMIBC and MIBC?

- Is there genetic predisposition for development/progression or treatment response
- Panels available UZ Leuven, MSK-IMPACT, Illumina
- Regarding existing risk models/calculators (EORTC/CUETO)

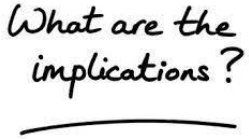
ATHENA – hurdles encountered

Legal framework

ATHENA as a **pilot** project for (secondary) use of RWD

In the setting of a VLAIO project

Needed a **specific trajectory** through ethical – data protection – legal departments/boards



Took **a lot of** time

ATHENA – hurdles encountered - achievements

Legal framework

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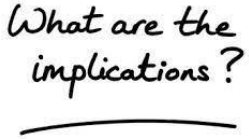


Took **a lot of** time

ATHENA – hurdles encountered - achievements

Legal framework

ATHENA as a **pilot** project for (secondary) use of RWD

In the setting of a VLAIO project

Needed a specific trajectory through ethical, data protection

BUT no approval for image analysis

What are the implications?

Took **a lot of** time

ATHENA – hurdles encountered

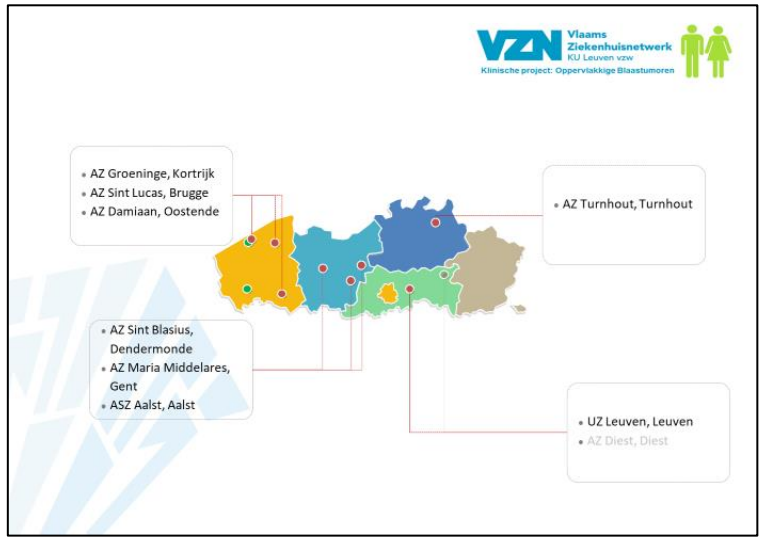
Data collection

Flemish bladder cancer registry

70-90% data completeness in **best** centers

other centers…

no data on MIBC or M+ BC



Data catalogue

link between EHR parameters and OMOP (also omic data)

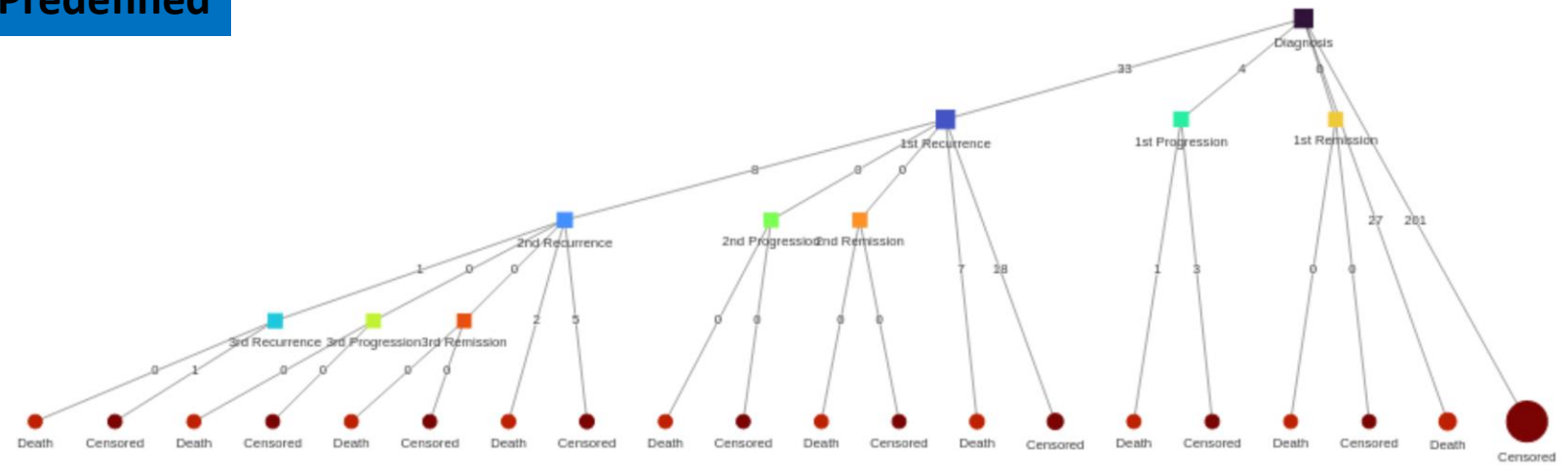
implies **choices**!

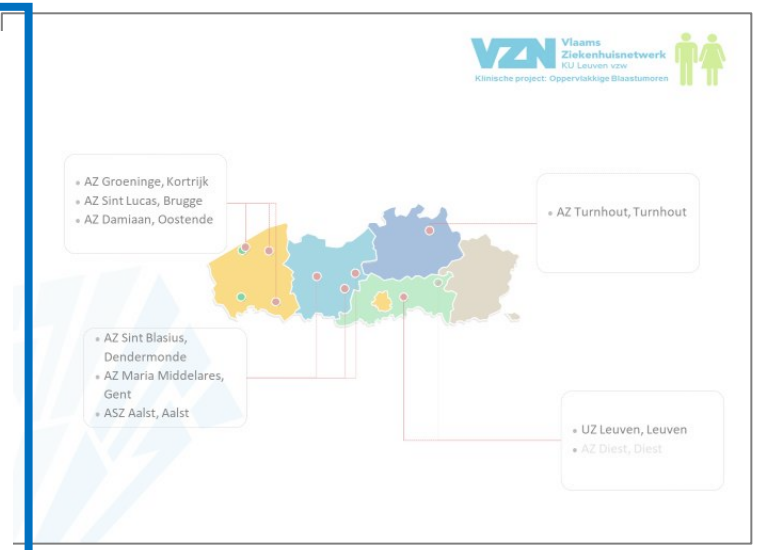
Data extraction

large datafiles, missing data,… → needs **manual** data iteration

ATHENA – hurdles encountered - achievements

Predefined





Dat

Work in Progress

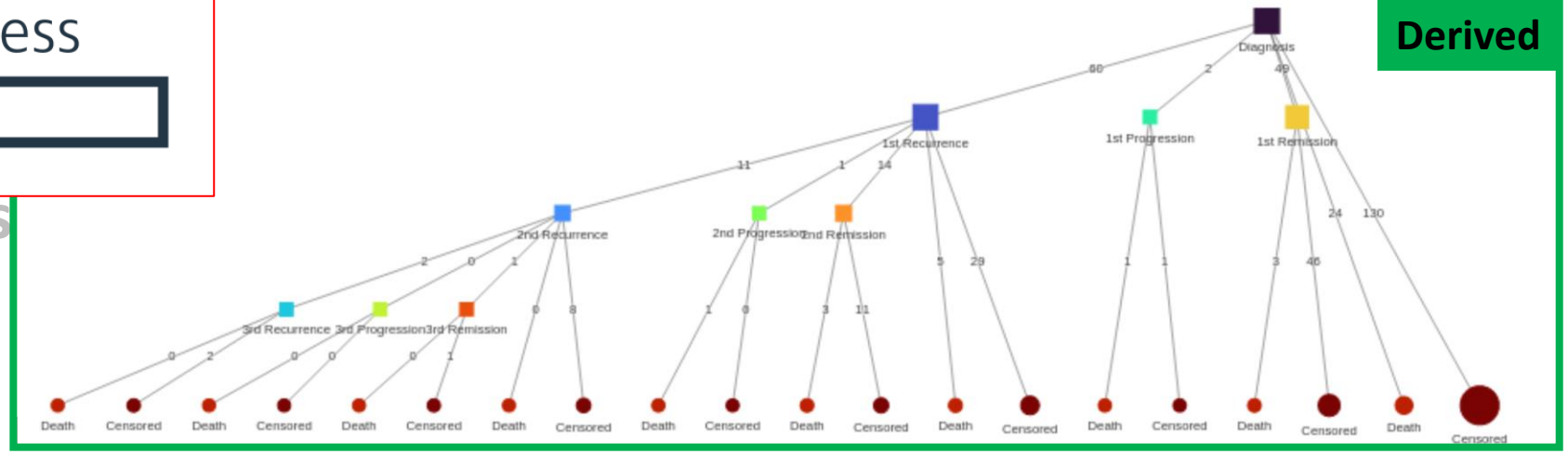
Loading...

implies **choices**

Data extraction

large datafiles,

Derived



ATHENA – hurdles encountered

Biobanking – omics data generation

Tissue collection in NMIBC can be **challenging**

- small lesions (enough tissue?)
- immediate processing
- not part of routine clinical practice

What are the implications?

→ Presence of research **personnel** required

→ Active cooperation of **surgeon** required

ATHENA – hurdles encountered

Biobanking – omics data generation

Omics data generated

- TSO 500 | 102 patients (retro)
- Bulk RNA seq
- analysis through available pipelines ongoing
- WP3

- methylation profiling ongoing (50%)
- single nucleus sequencing planned (Q1 2024)

→ Active cooperation of **surgeon** required

Conclusions

(NMI)BC is a challenging case that fits well in the scope of the ATHENA project

Many hurdles taken, but several hurdles ahead

We are not running a sprint, but a marathon

ATHENA can serve as a baseline project

ATHENA = teamwork

UZ Leuven team

Murat Akand

Jan Cornelissen

Andries Clinkaert

Loic Baekelandt

all CABLE participants

all clinicians that use(d) forma

Agnes Van den Berghe, Ann Lis

Hilde Steeno

…

Genomics Core

Tatjana Jatsenko

Marian Crabbé

Joris Vermeesch

…

JNJ

Flavio Cammarone

Michel Van Speybroeck & team

Bart Vannieuwenhuyse

Tinne Lewi

Patricia Van Rompuy

Valerie Vandeweerd

Dario Masullo …

And many more…

UZ LEUVEN

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