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Predictive biomarkers for MIBC and NMIBC

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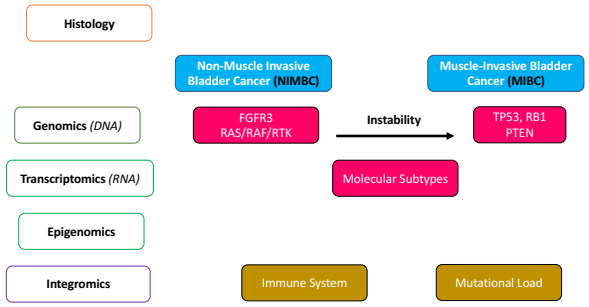
Recommendation	Strength rating
Do not use biomarkers in daily clinical practice since they have no impact on predicting outcome, treatment decisions, or monitoring therapy in muscle-invasive bladder cancer.	Strong

EAU Guidelines MIBC 2018

"A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes or responses to an exposure or intervention."[1]

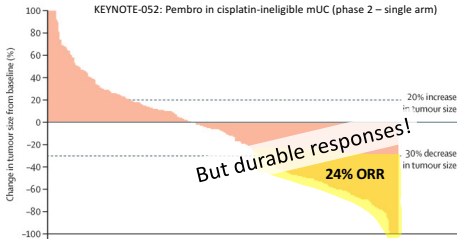
- **Diagnostic**
- **Prognostic** – *~ Disease outcome* → Who to treat?
- **Predictive** – *~ Therapy effect* → How to treat?

1. FDA-NIH Biomarker Working Group (2016)
Courtesy of Thomas Gevaert (KU Leuven/ AZ Klina)



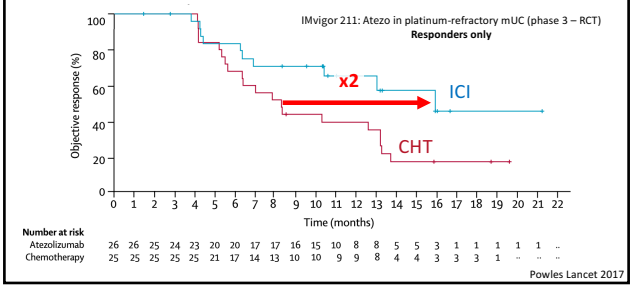
Why do we need predictive biomarkers

Patient selection – not all patients respond



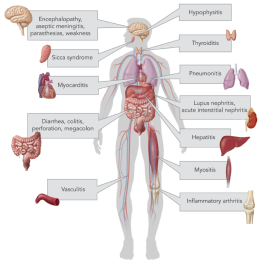
Balar, Lancet 2017

But more durable responses than CHT



Powles Lancet 2017

New therapies – different adverse event profiles



Common Immune-Related AE by Organ System– Brook Coppola

New therapies – durable responses at what cost

Costs in Belgium 11/2019
Source: BCFI.be/CBIP.be

Predictive biomarkers allow for

- Patient selection
- Reduce adverse events
- Decrease costs

Predictive biomarkers for BCG

NMIBC

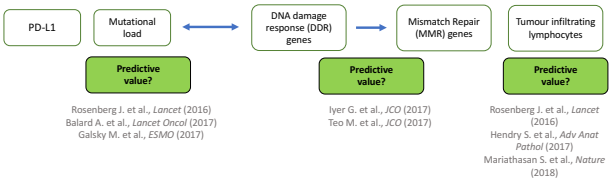
Why?	30-50% BCG failures	BCG = golden standard
What?	Urinary cytokines[1-5]	Mutational load[6]
Problem!	No validation in RCT setting	No interest industry

1. Saint J Urol 2002 2. Watanabe Canc Immun 2003, 3. Kumar J Urol 2002, 4. Thalmann J Urol 2019, 5. Kamat EU 2016, 6. Bastos JCO 2019

Predictive biomarkers for immunotherapy

MIBC

Biomarkers for immunotherapy

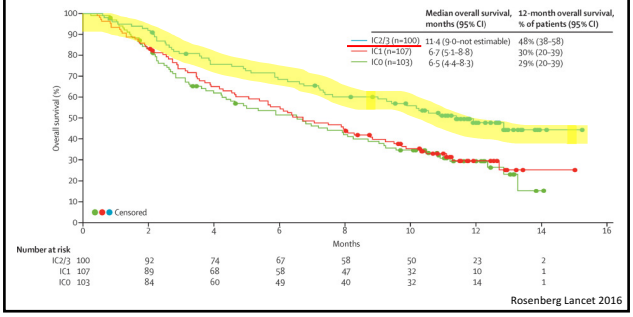


Rosenberg J. et al., *Lancet* (2016)
Balard A. et al., *Lancet Oncol* (2017)
Galsky M. et al., *ESMO* (2017)

Iyer G. et al., *JCO* (2017)
Teo M. et al., *JCO* (2017)

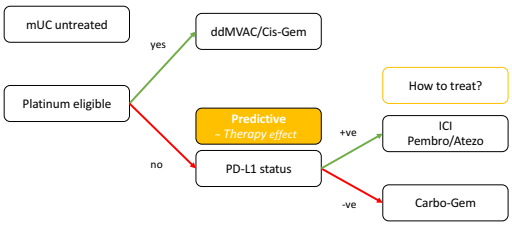
Rosenberg J. et al., *Lancet* (2016)
Hendry S. et al., *Adv Anat Pathol* (2017)
Mariathasan S. et al., *Nature* (2018)

IMvigor 210: Atezo in platinum-treated progressive mUC (phase 2 – single-arm)

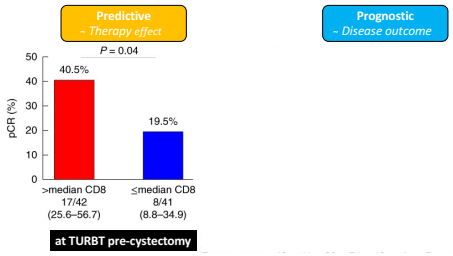


Rosenberg Lancet 2016

Treatment in first-line setting chemo-naïve mUC



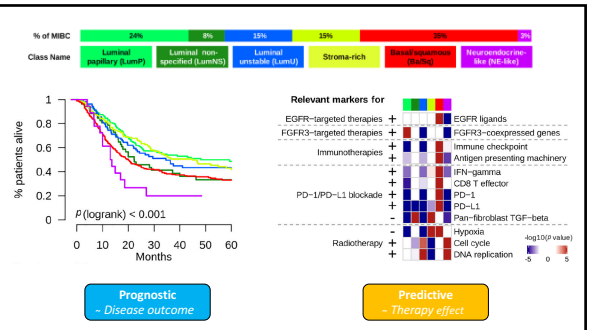
ABACUS - neoadjuvant ICI before RC

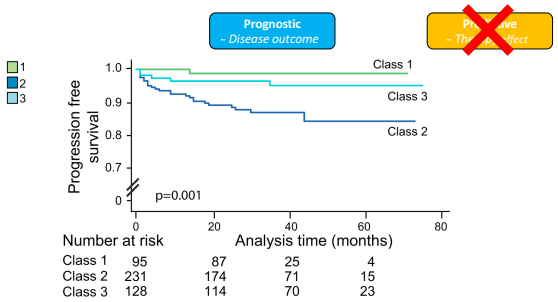


Powles Kockx Nature Medicine 2019

Molecular subtypes as biomarker

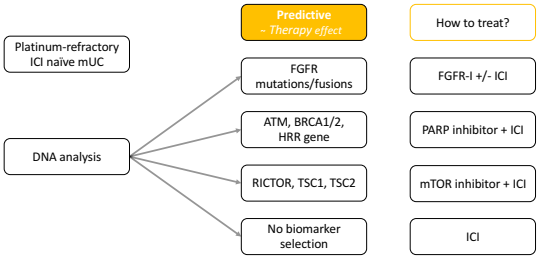
MIBC and NMIBC





Hedegaard 2016 Cancer Cell

Validation of predictive biomarkers



ESMO 2019, Powles

Negative trial – approach is feasible

	FGFR-I	FGFR-I + ICI	PARP-I + ICI	mTOR-I + ICI	ICI
Patients (n)	15	21	14	29	29
ORR	20%	29%	36%	24%	28%
PD-L1 status +ve	25%	23%	50%	50%	54%
tTMB high > 10	23%	5%	54%	43%	18%

No combination of treatments and biomarker selection reached the prespecified efficacy target… ORR >60%

But: trial shows feasibility of the approach!

ESMO 2019, Powles

Conclusions

Predictive biomarkers are necessary

Existing predictive biomarkers are not perfect

Clinical trials incorporating biomarkers are initiated

Renowned focus on BCG is needed!