

ITCC EDUCATION MEETING UTRECHT

Workshop 5 – Simulated Molecular Tumor Board

Introduction

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Aim: prioritize 1-2 actionable lesions from DNA/RNA sequencing data

- Example 1: acute lymphoblastic leukemia
- Example 2: rhabdomyosarcoma
- Example 3: neuroblastoma
- Example 4: neuroblastoma

Time schedule for workshop (45')

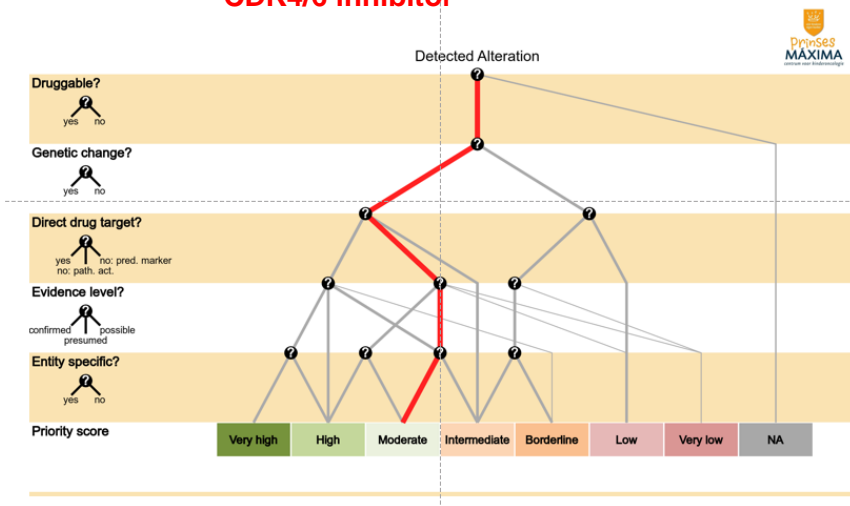
- Introduction (5')
- Split up in small groups according to color (5')
- Discussion of example case per group (15')
- Presentation to the whole group (5' x 4 examples)

Have fun!

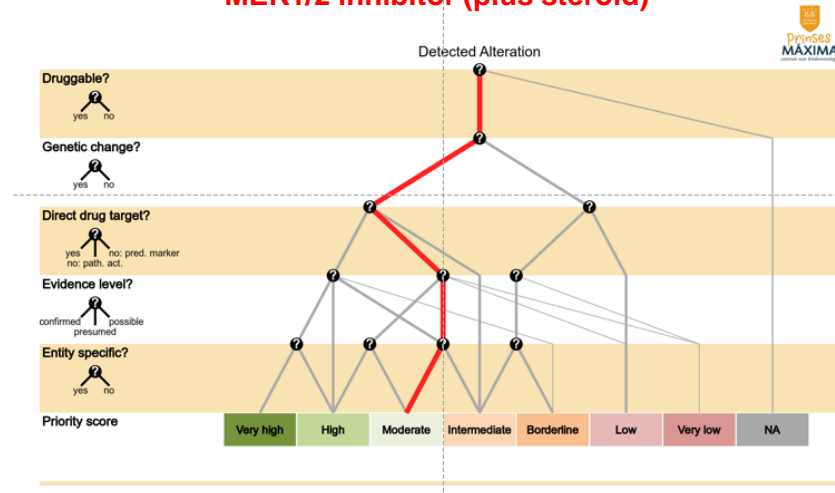
Solution 1: T-cell ALL

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Actionable event 1: CDKN2A/B homozygous deletion CDK4/6 inhibitor



Actionable event 2: IL7R mutation MEK1/2 inhibitor (plus steroid)



Alteration Type	Action of Drug	Target Type	Entity	Priority
Genetic	Pathway	Presumed pathway activation	Specific	3. Moderate

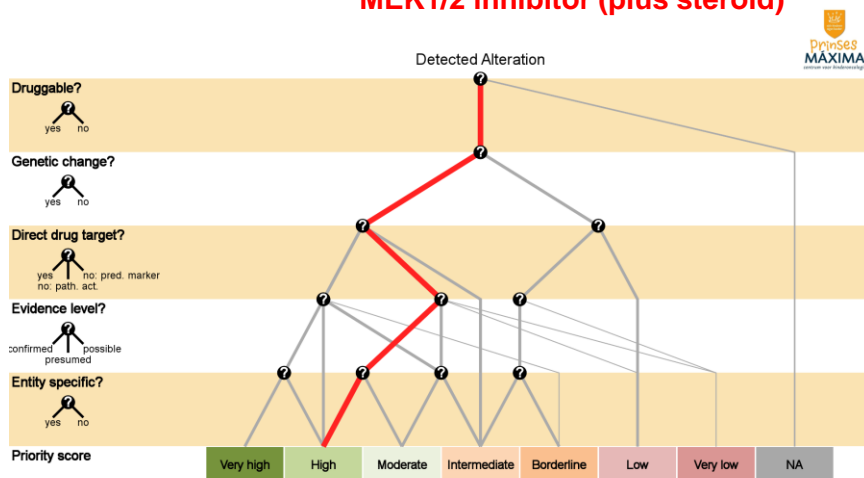
Alteration Type	Action of Drug	Target Type	Entity	Priority
Genetic	Pathway	Presumed pathway activation	Specific	3. Moderate

The actionable events are probably not the primary oncogenic driver; treatment with single compound likely to result in resistance. Patient is being treated with standard chemotherapy to bridge to stem cell transplantation.

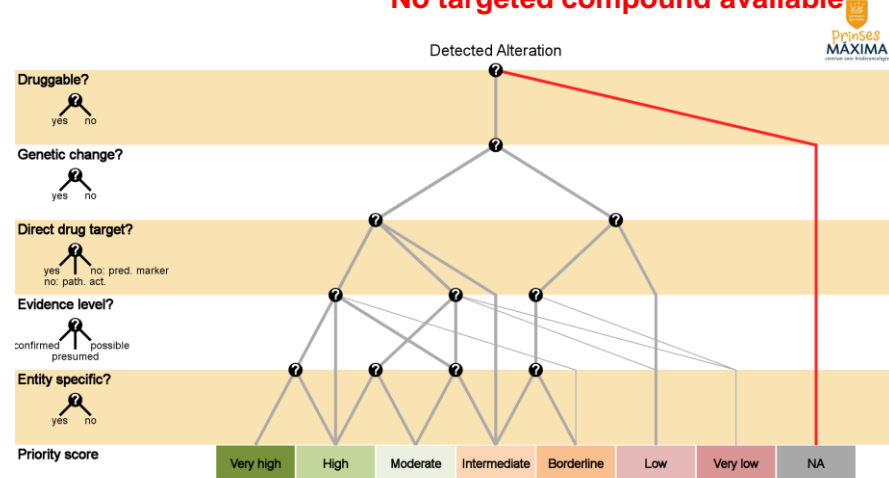
Solution 2: Rhabdomyosarcoma

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Actionable event 1: **KRAS amplification** **MEK1/2 inhibitor (plus steroid)**



Actionable event 2: **TP53 mutation** **No targeted compound available**



Alteration Type	Action of Drug	Target Type	Entity	Priority
Genetic	Pathway	Confirmed pathway activation	Specific	2. High

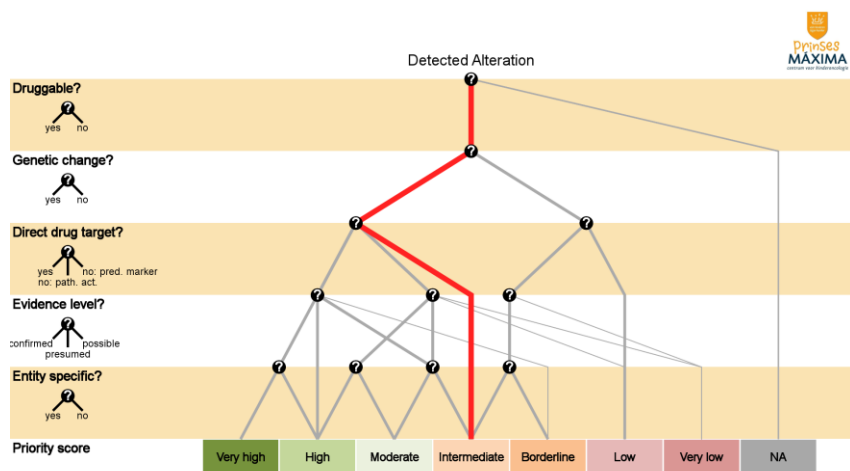
Alteration Type	Action of Drug	Target Type	Entity	Priority
Genetic	Any	Biological interest	Any	8. NA

The TP53 mutation was somatic; reminder that sequencing can uncover germline mutations associated with cancer predisposition syndromes (e.g. Li-Fraumeni).

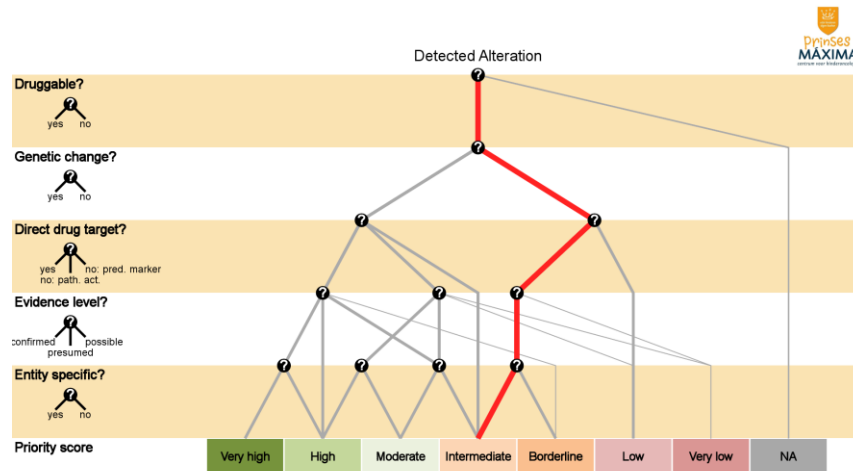
Solution 3: Neuroblastoma

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Actionable event 1: MYCN amplification PI3K/AURKA/HDAC inhibitor



Actionable event 2: BCL2 overexpression BCL2 inhibitor



Alteration Type	Action of Drug	Target Type	Entity	Priority
Genetic	Sensitizing	Any	Any	4. Intermediate

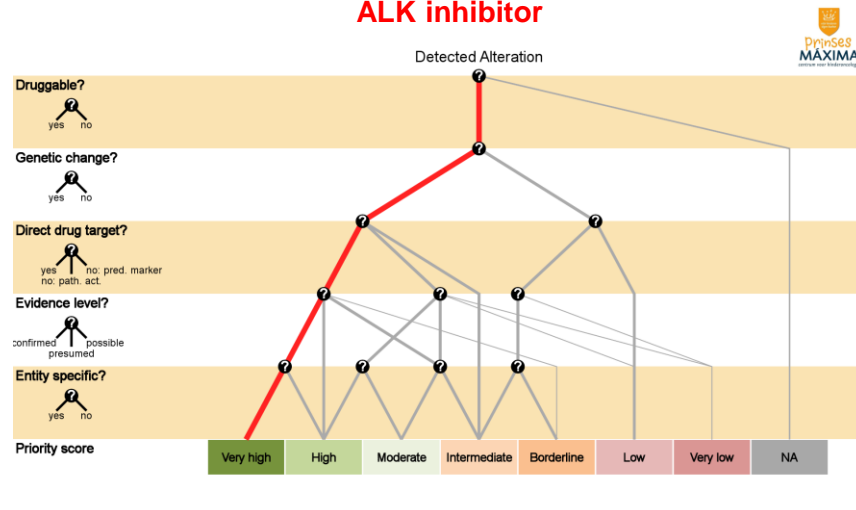
Alteration Type	Action of Drug	Target Type	Entity	Priority
Expression	Direct	Confirmed	Specific	4. Intermediate

MYCN is a high risk marker but not a good actionable target. BCL2 inhibitor may work, but priority is Intermediate because the expression change is not a genetic alteration.

Solution 4: Neuroblastoma

Solution 4: Neuroblastoma

Actionable event 1: **ALK mutation** **ALK inhibitor**



Alteration Type	Action of Drug	Target Type	Entity	Priority
Genetic	Direct	Confirmed	Specific	1. Very high

Activating mutation in a confirmed driver that is specific for neuroblastoma.
Actionable events with Very high priority are likely to be introduced in first line therapy.