

Myeloma: Future Directions

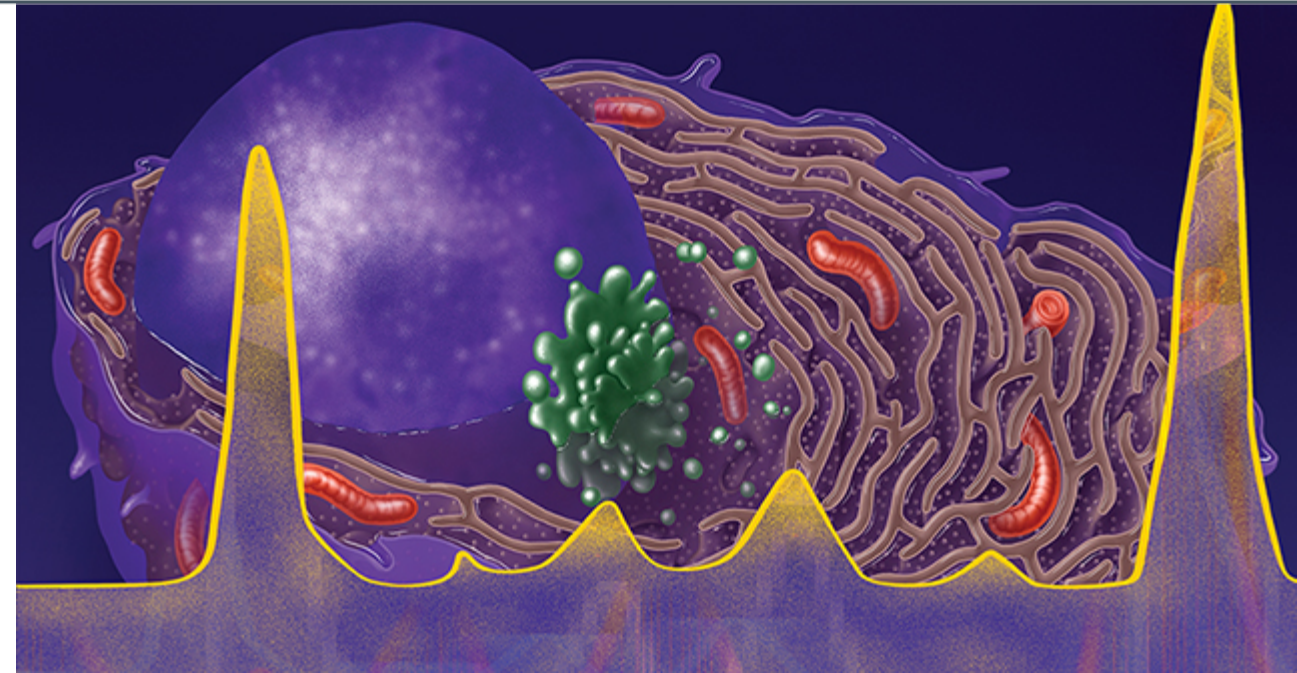
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Myeloma: Future Directions

S. Vincent Rajkumar
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Scottsdale, Arizona



Rochester, Minnesota



Jacksonville, Florida

No conflicts to disclose

New Anti-CD38 antibodies

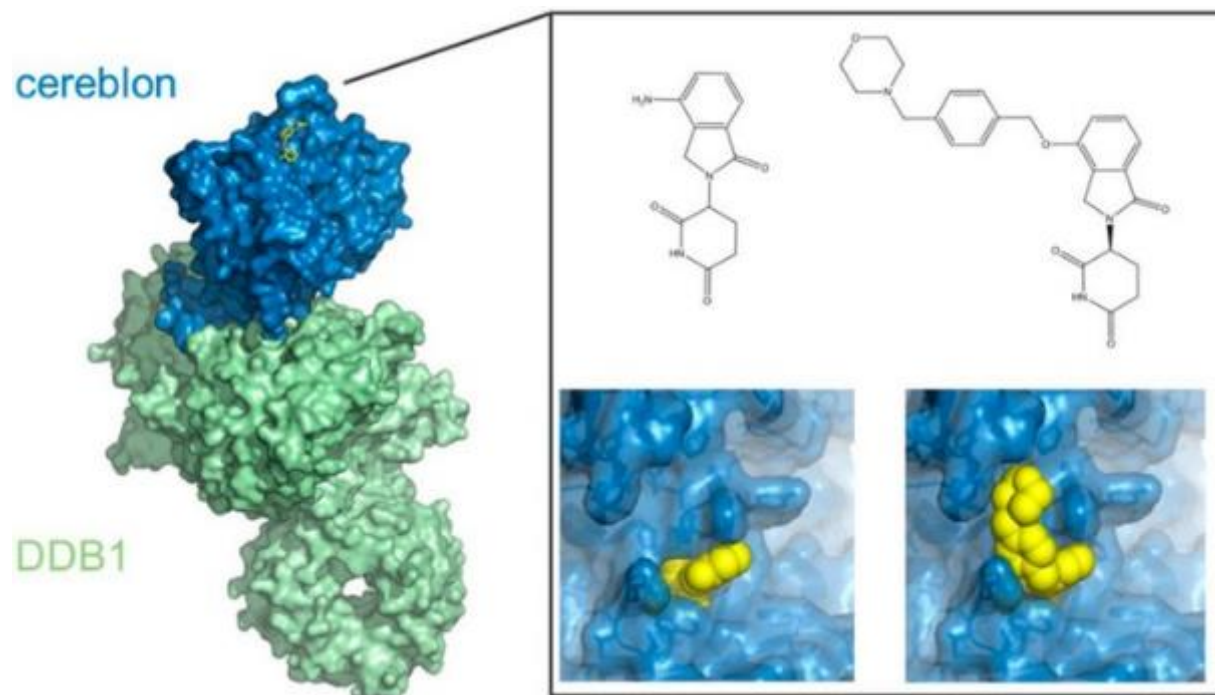
- **TAK-079**
- **MOR 202**
- **SAR 442085**

- **Problem: Resistance**
- **Abstract 721: Biallelic loss of BCMA (del 16p)**

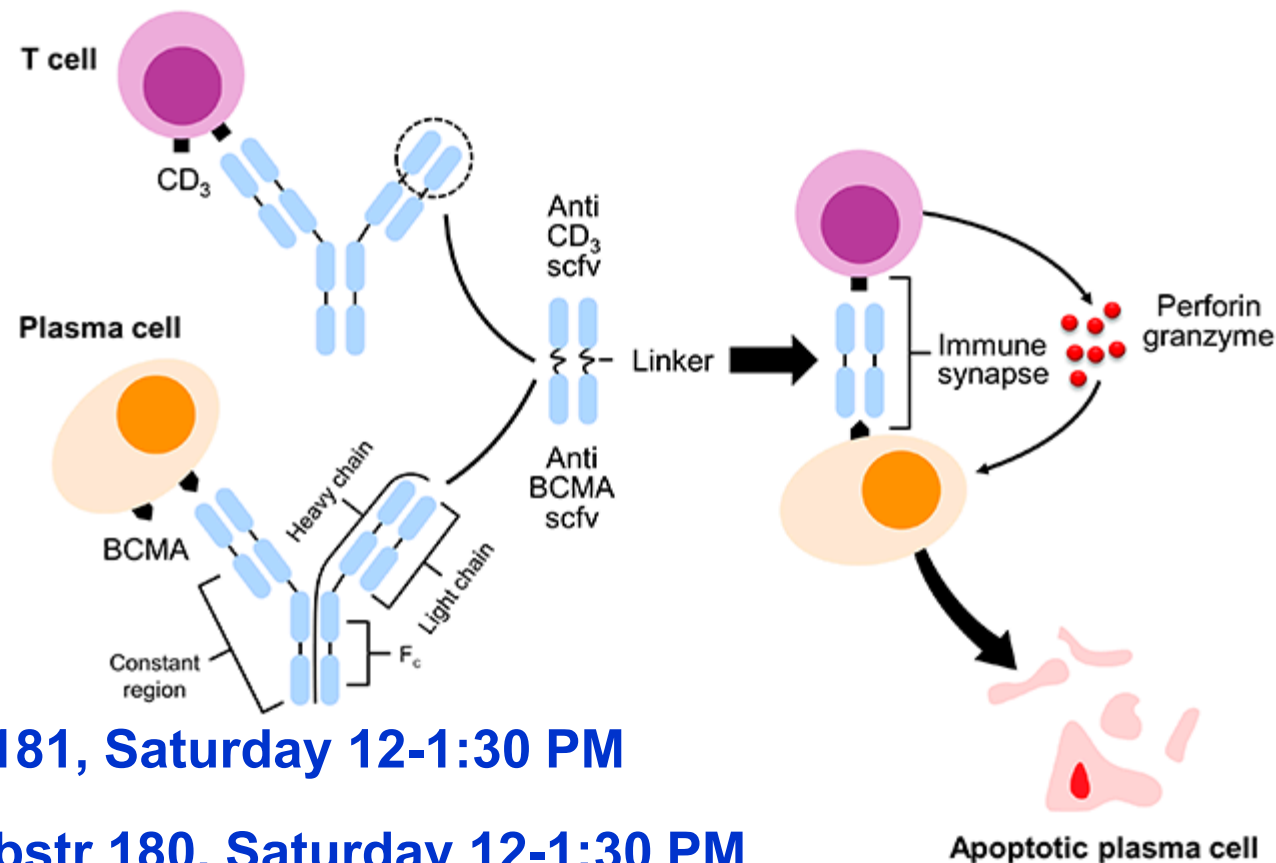
Newer IMiDs/Cel Mods

- **Iberdomide (CC-220) (Cereblon ligase modulator)**
 - ASH 2020 Abstract 724: First Results of Iberdomide + Dara/Dex or Iberdomide + Vd in RR MM

- **CC-92480**



Bispecific Antibodies



AMG 701: Abstr 181, Saturday 12-1:30 PM

Teclistamab: Abstr 180, Saturday 12-1:30 PM

CC 93269

Novel Bispecifics

BFCR4350A: Bispecific targeting FcRH5 and CD3

- **Cohen et al, Abstract 292: Saturday Dec 5, 2-3:30 PM**

Talquetamab: Bispecific targeting GPRC5D and CD3

- **Chari et al, Abstract 290: Saturday Dec 5, 2-3:30 PM**

Novel CAR-T Approaches

Earlier disease setting

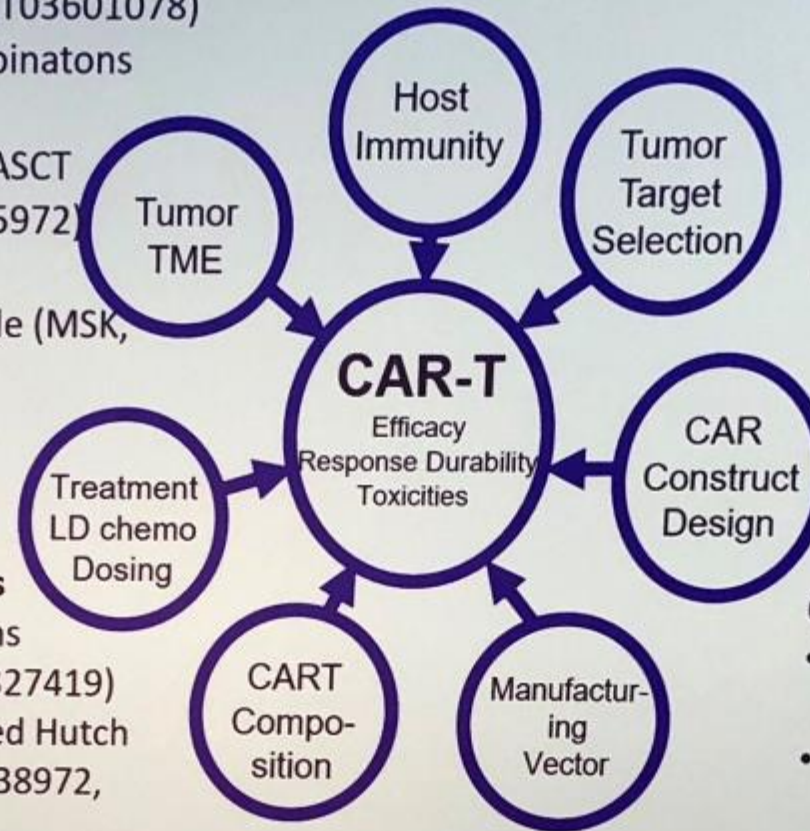
- Early relapse (bb2121, NCT03601078)
- Randomized vs Dara combinatons (bb2121, NCT03651128)
- BCMA + CD19 CART post ASCT (NCT03549442, NCT03455972)

Combination approaches

- BCMA CART + lenalidomide (MSK, NCT03070327)

CAR-T Composition Strategies

- Memory like T cell functions (bb21217, BlueBird, NCT0327419)
- Defined CD4/CD8 ratio (Fred Hutch & JACR125, JUNO, NCT03338972, NCT03430011)
- CD8 only (Cartesian Therapeutics, NCT03448978)



Antigen targets

- APRIL CAR (Autolus, NCT032878)
- CS-1 (NCT03710421)
- NKG2D-ligands (NCT02203825)
- CD38 (Sorrento, NCT03464916)

Modulate tumor antigen expression

- BCMA CART with gamma-secretase inhibitor to increase BCMA expression (NCT03502577)

CAR-T Constructs

- CARTyrin, transposon (Poseida, NCT03288493)
- BCMA mAb + Fc CART (Unum Therapeutics, NCT03266692)

Allogeneic UCART

- BCMA (NCT03752541)

Novel CAR-T

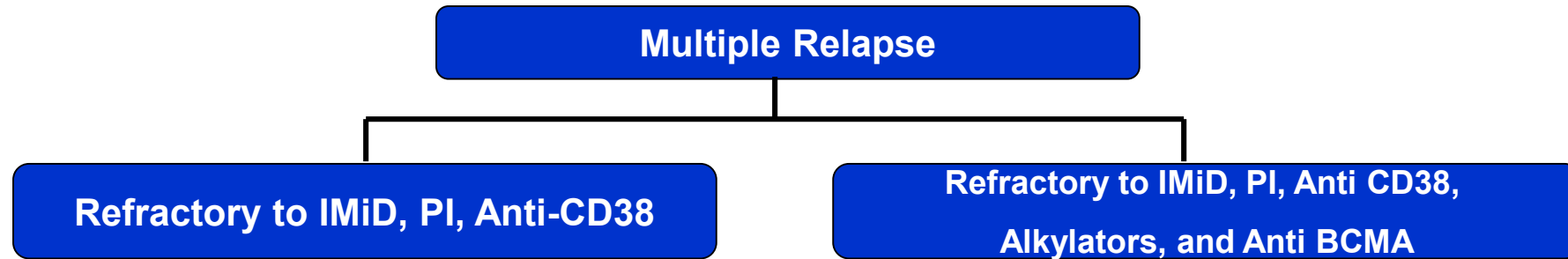
ALLO-647: allogenic, off-the-shelf CAR-T

- **Mailankody, et al. Abstract 129: Saturday, Dec 5 9:30-11 AM**

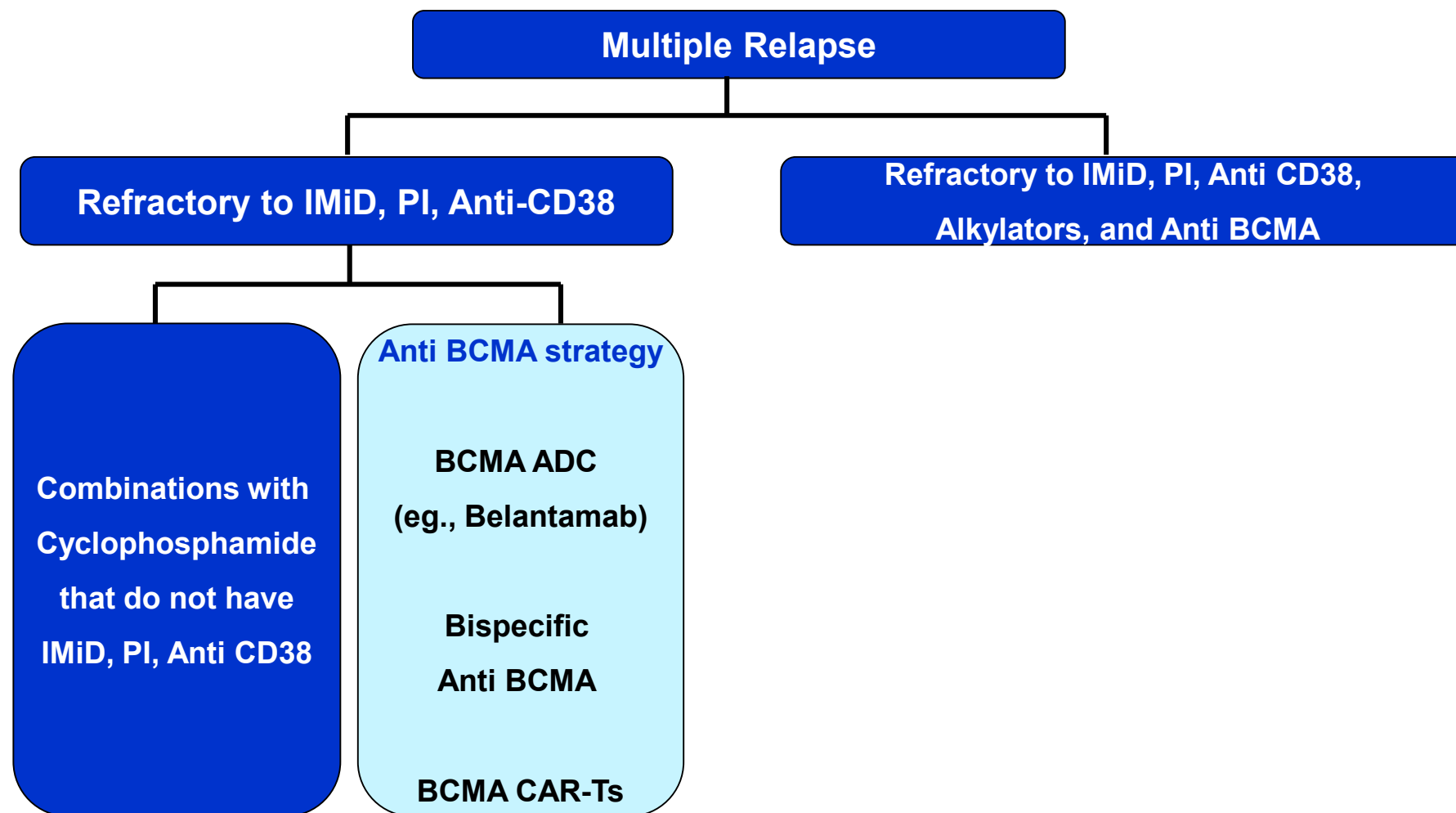
Other approaches

- **Combined CD19-BCMA**
- **Multiantigen targeting**
- **Individualized targeting**
- **CAR-NK**

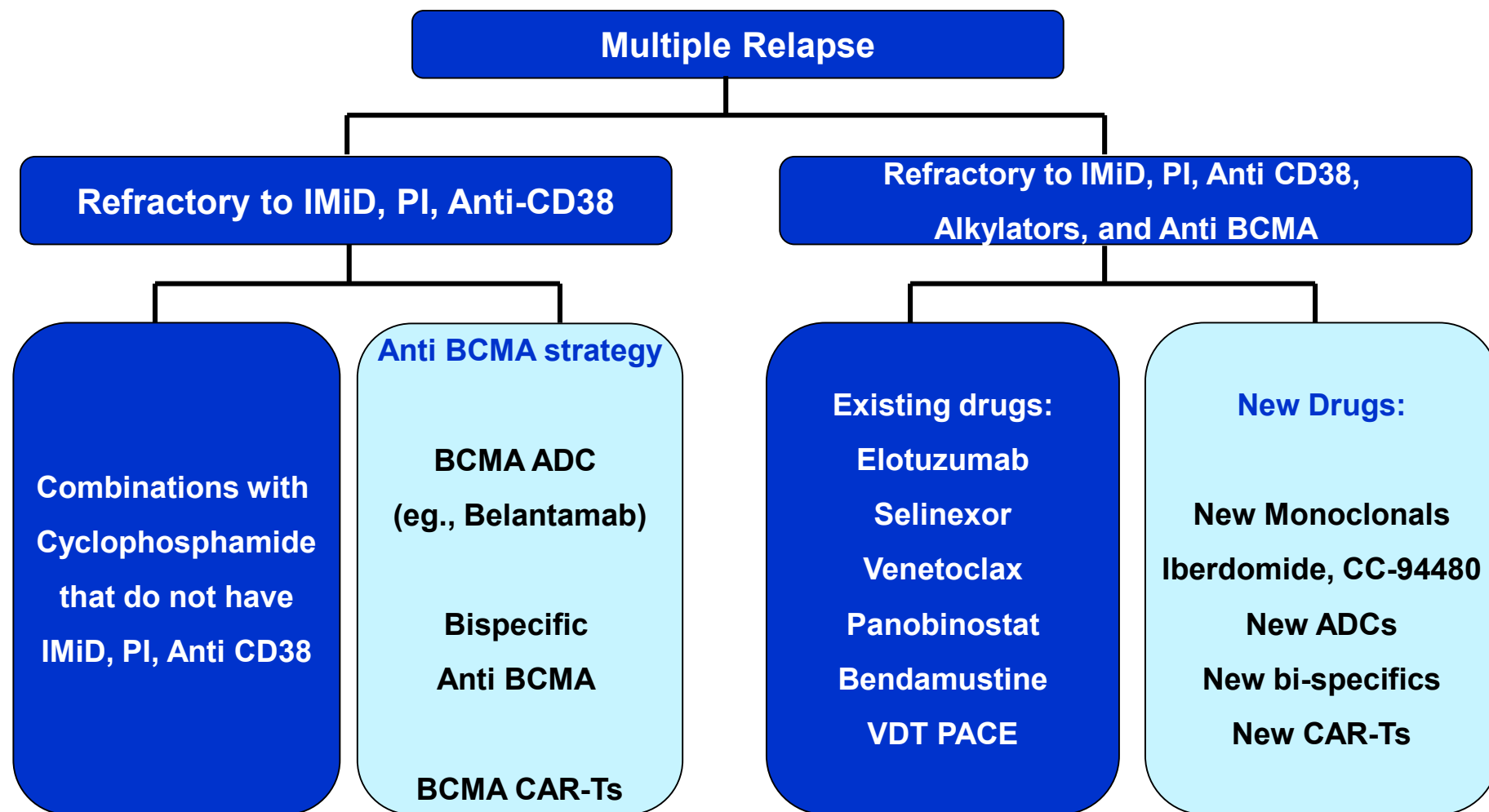
Myeloma: Future State



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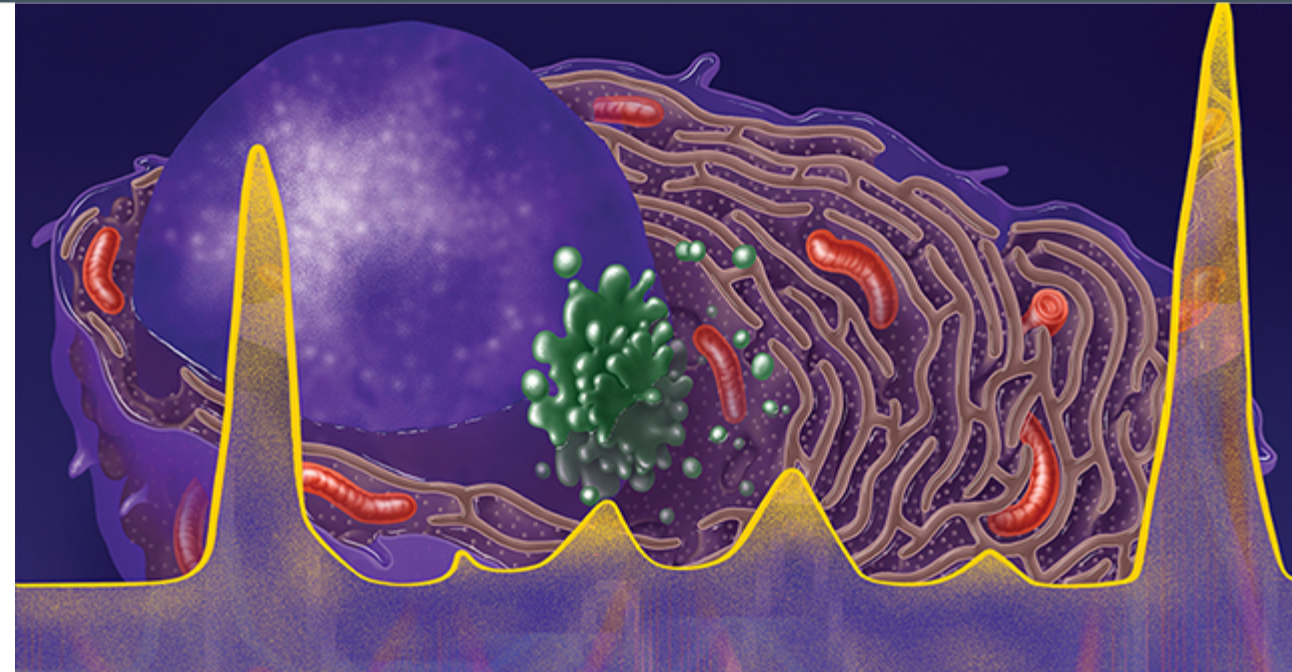


Panel Discussion: Future Directions for Myeloma



Proposed 2021 Treatment Algorithms

Panel Discussion



When Should Treatment Be Initiated?

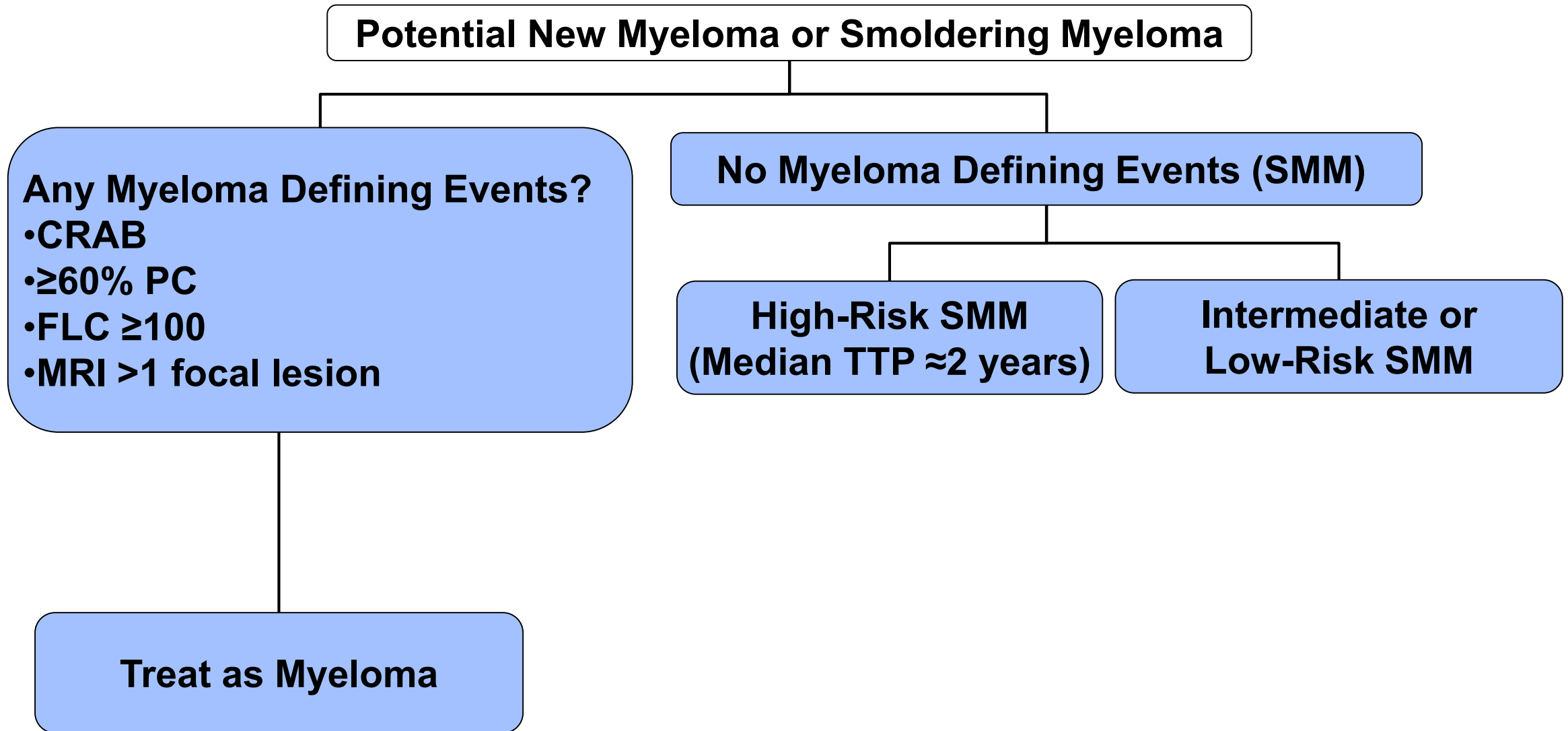
Potential New Myeloma or Smoldering Myeloma

Any Myeloma Defining Events?

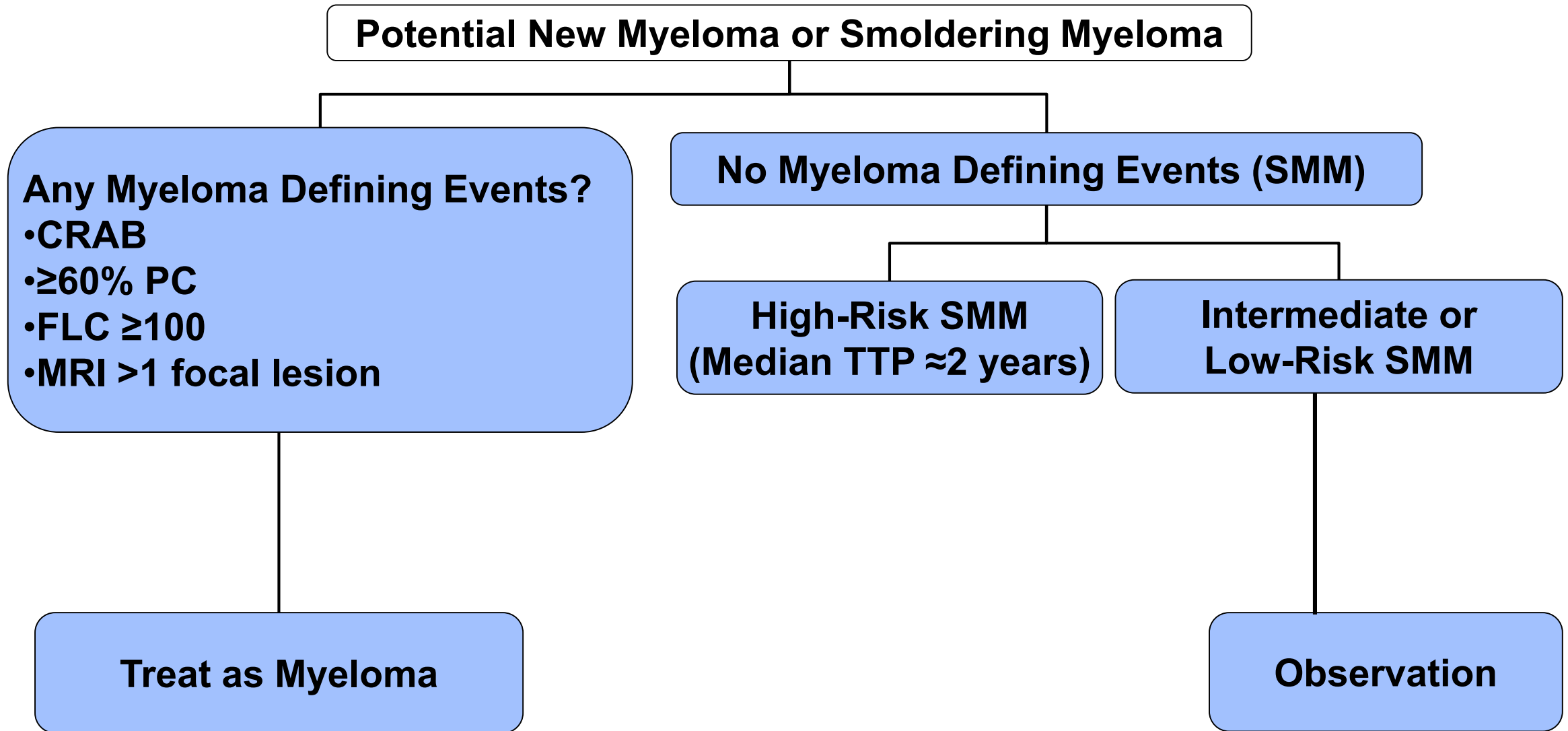
- CRAB
- $\geq 60\%$ PC
- FLC ≥ 100
- MRI > 1 focal lesion

Treat as Myeloma

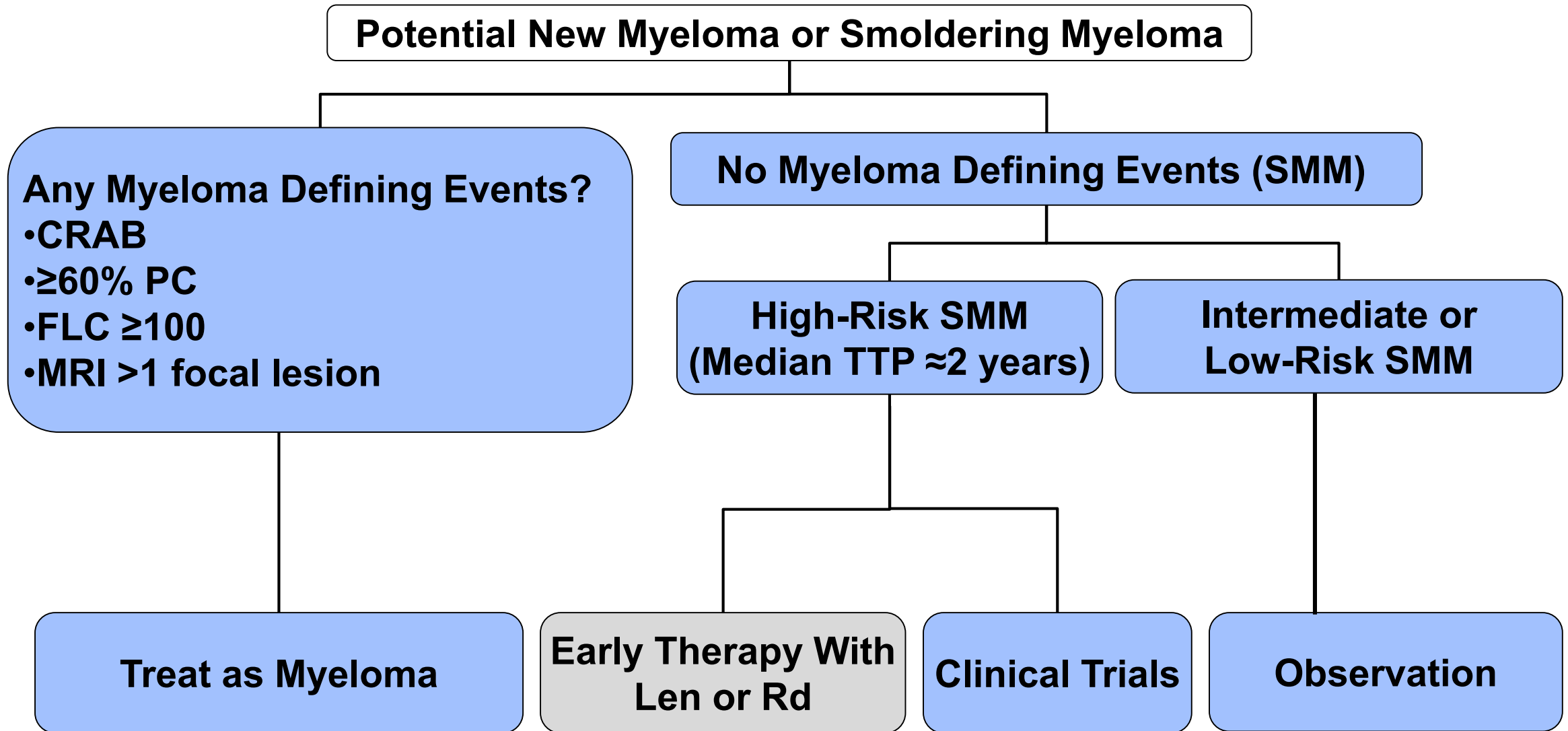
When Should Treatment Be Initiated?



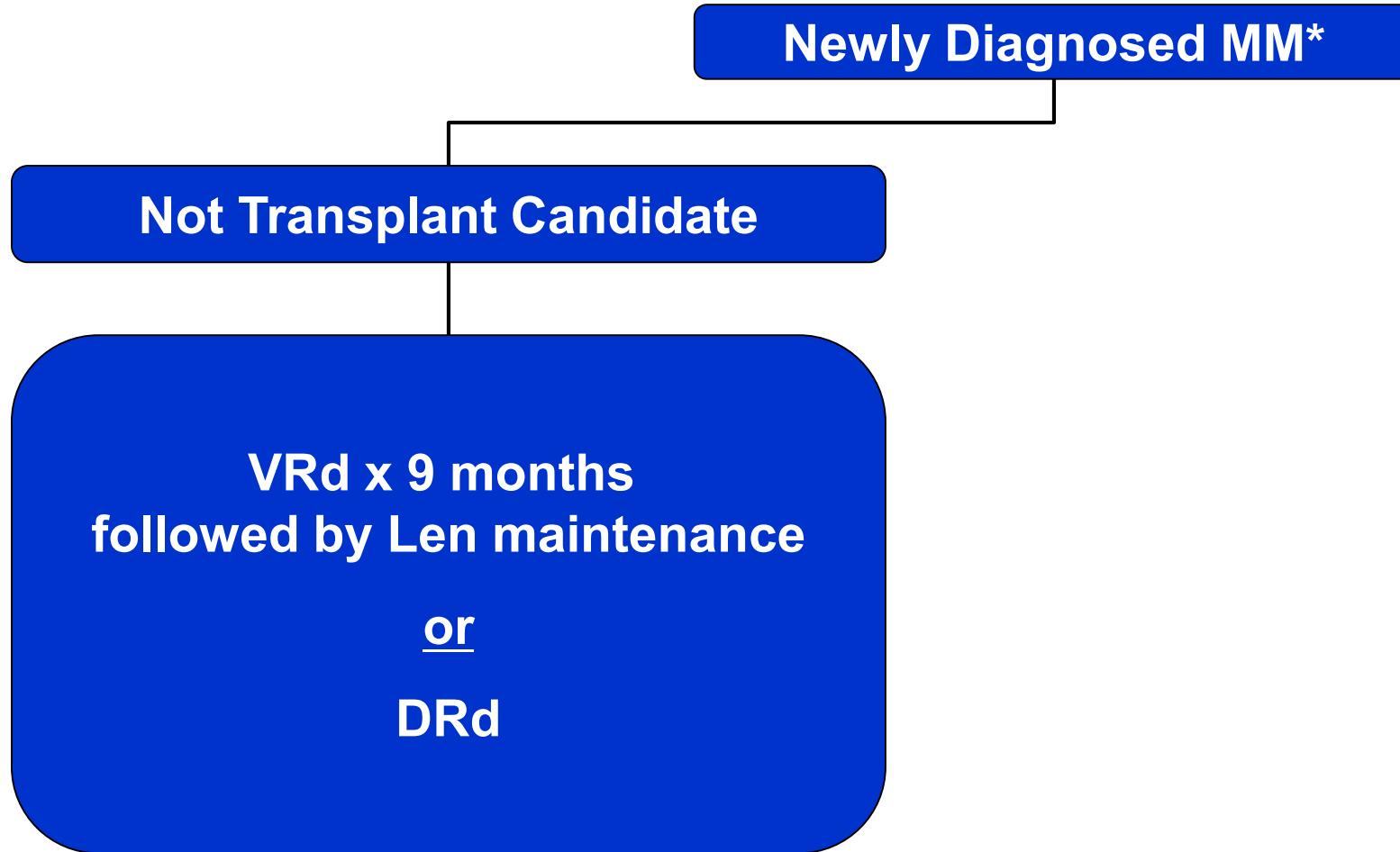
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When Should Treatment Be Initiated?



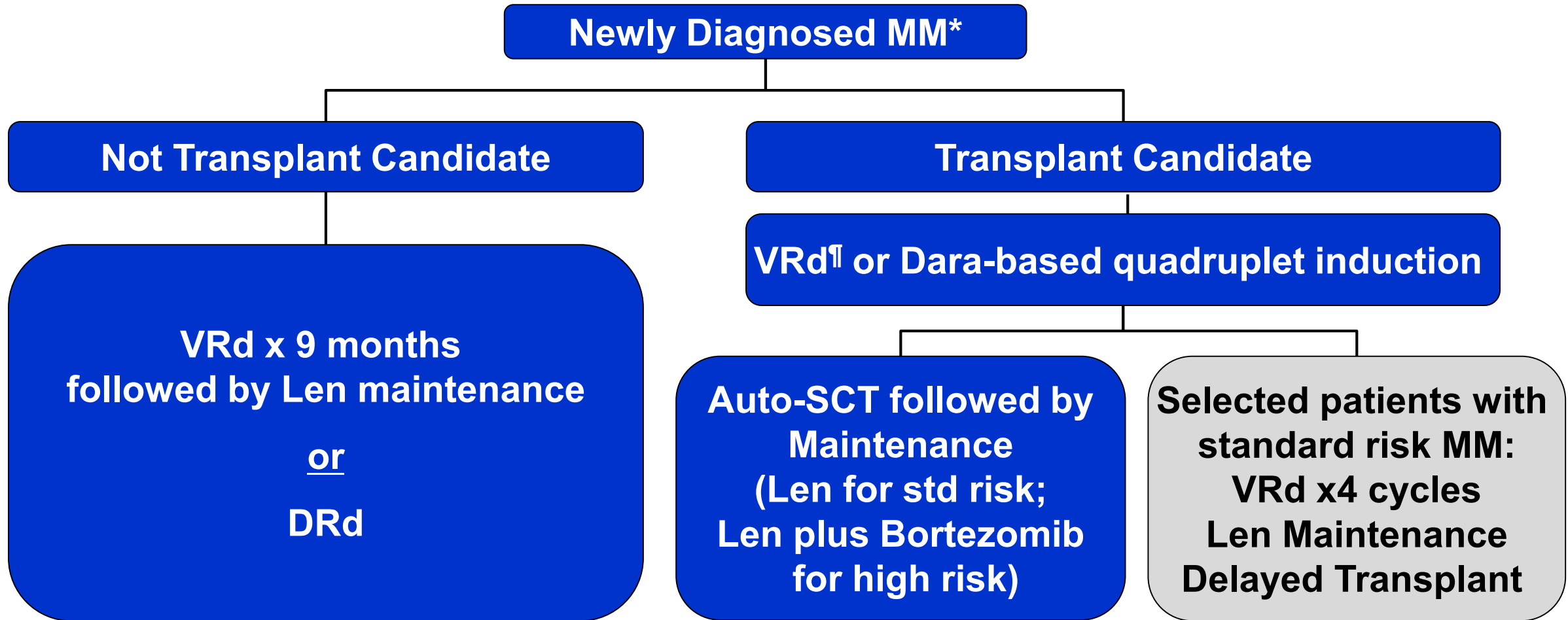
Myeloma: Frontline Treatment



*Based on CALGB 100104, S0777, IFM-2009, CTN 0702, HOVON, MAIA, CASSIOPEIA

† VTd/VCd if VRd not available

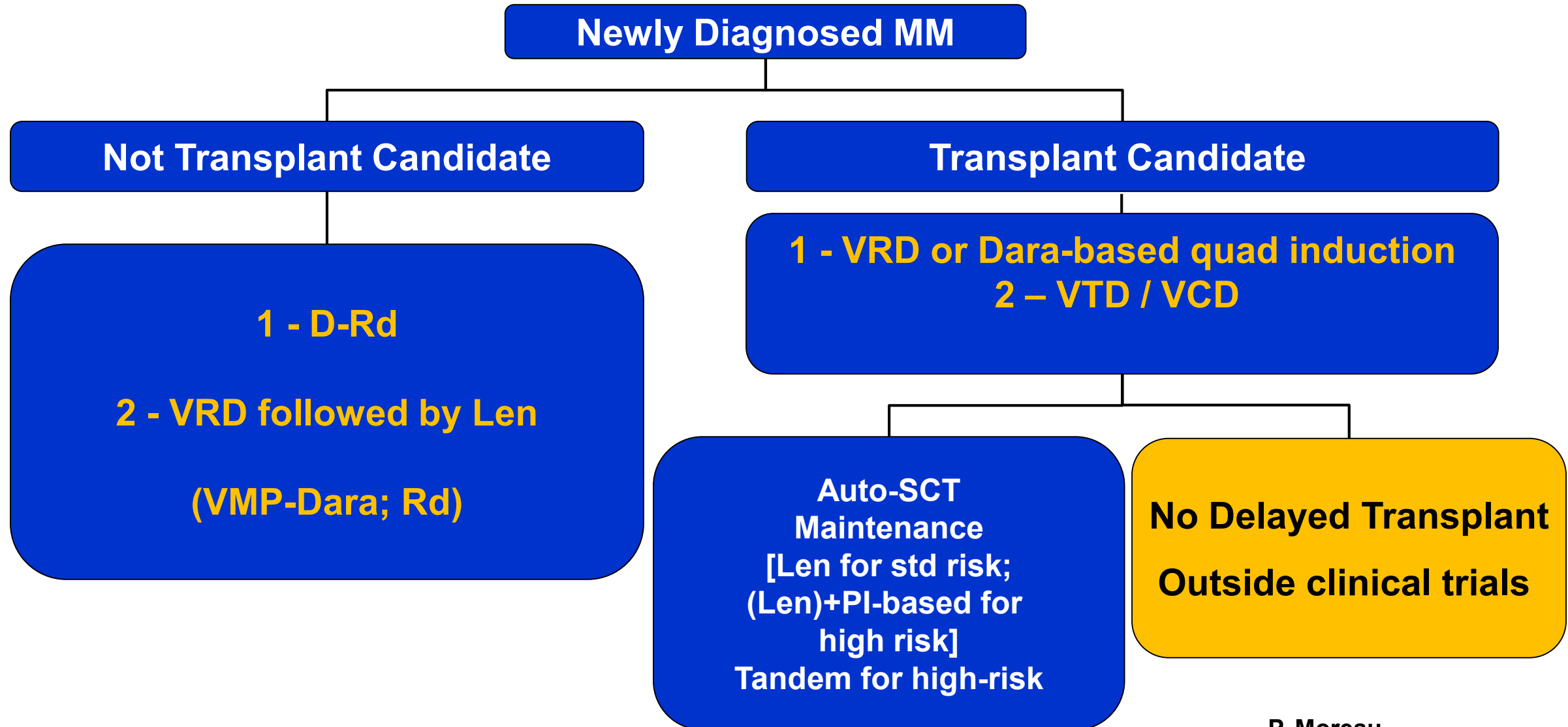
Myeloma: Frontline Treatment



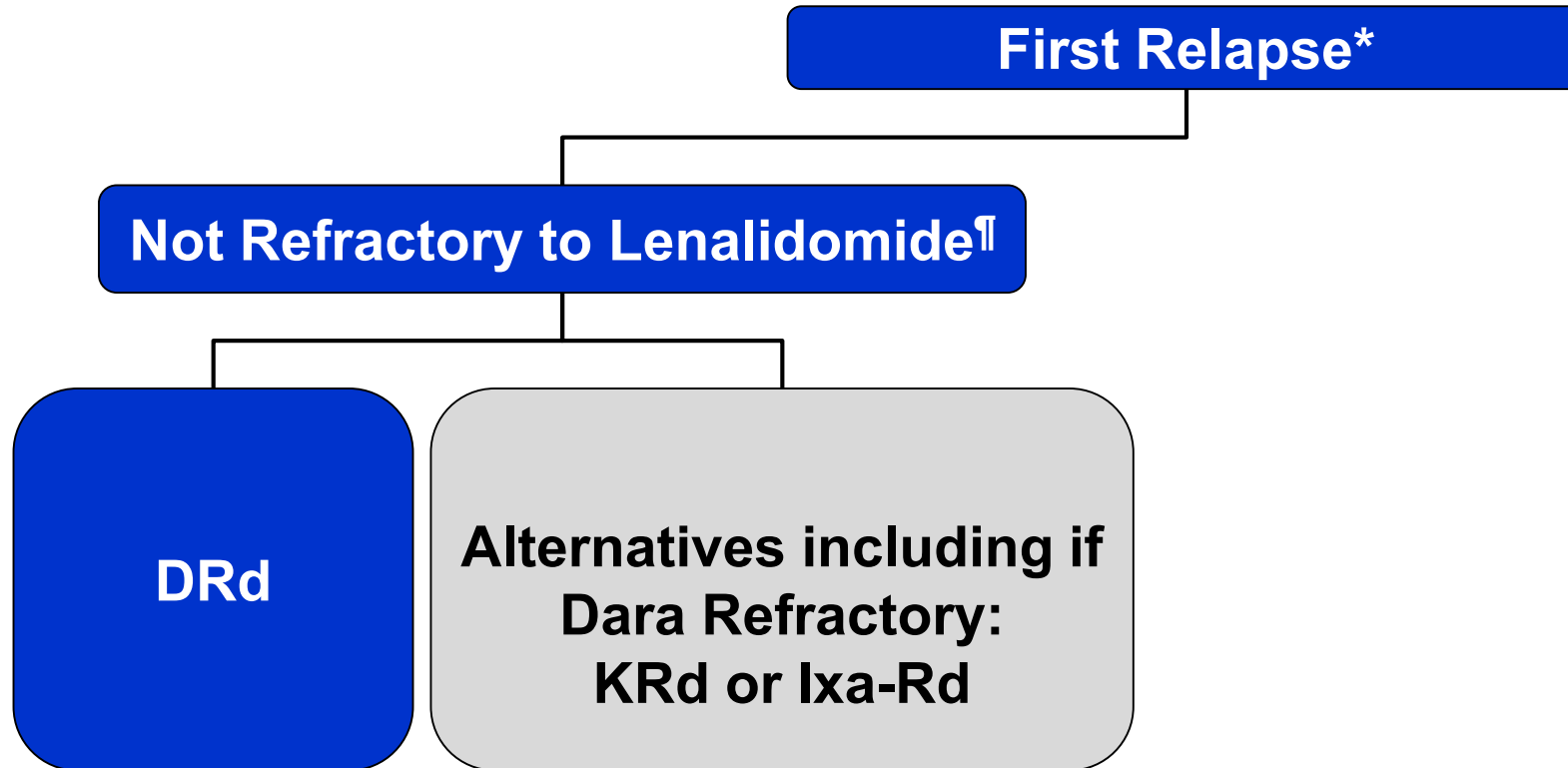
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Myeloma: Frontline Treatment



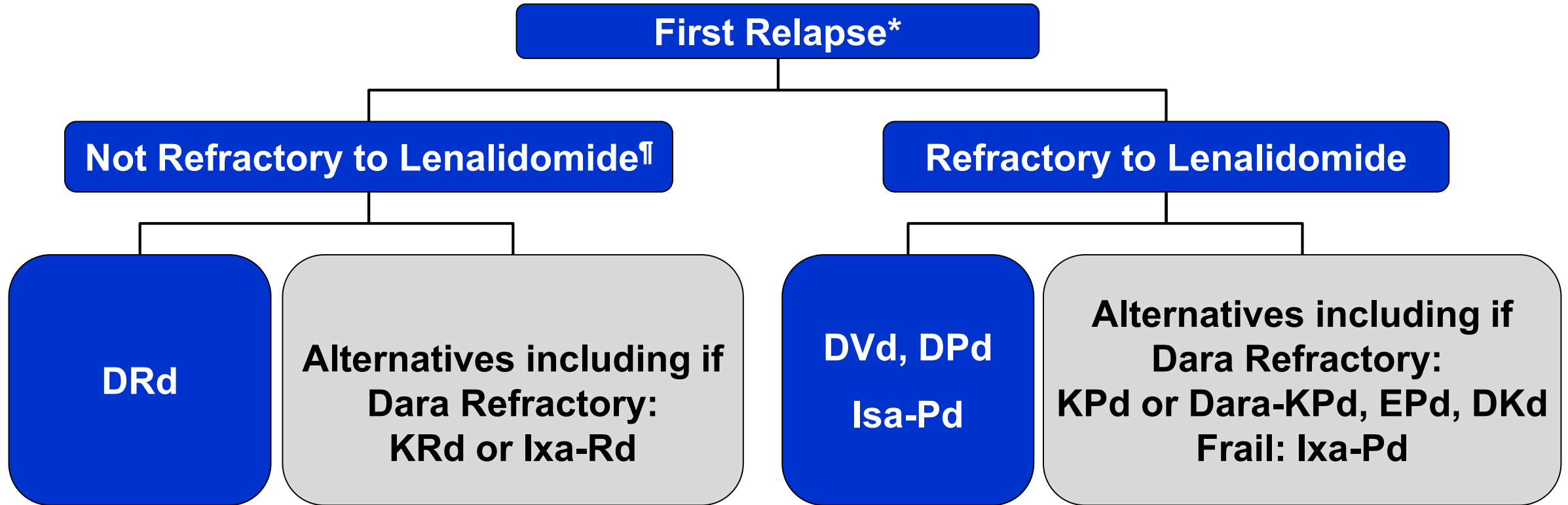
Myeloma: First Relapse



*Consider salvage auto transplant in eligible patients

†Relapse occurring while off all therapy, or while on small doses of single-agent lenalidomide, or on bortezomib maintenance

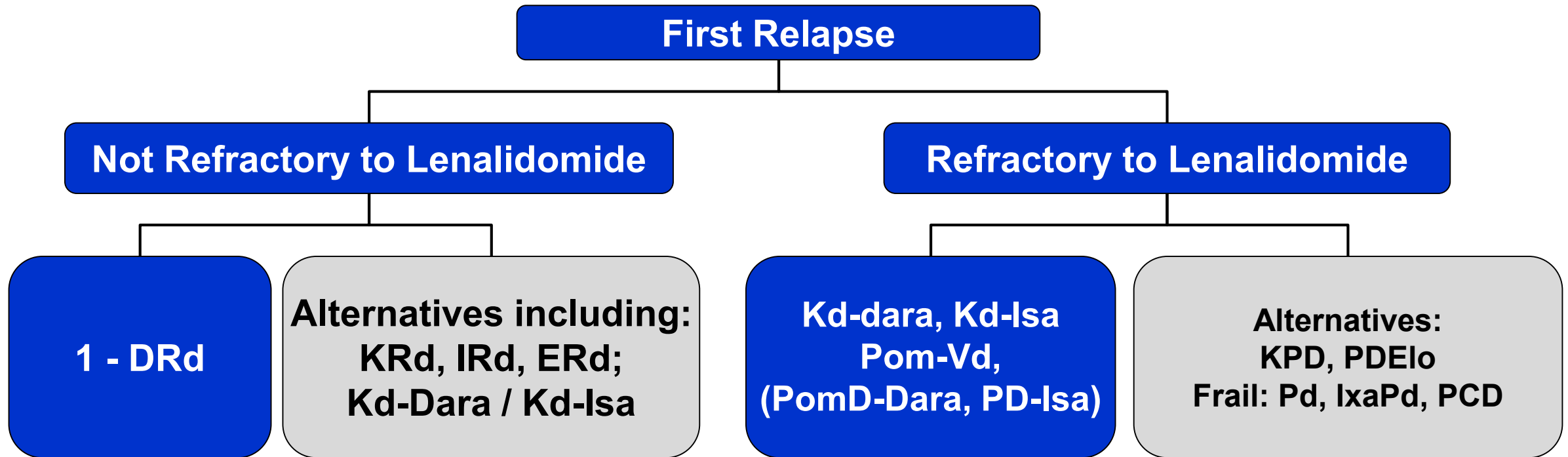
Myeloma: First Relapse



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Myeloma: First Relapse



! Challenge : patients progressing on frontline dara

Myeloma: Second or Higher Relapse

First Relapse Options



- **Any first relapse options that have not been tried**

**(2 new drugs;
triplet preferred)**

Myeloma: Second or Higher Relapse

First Relapse Options



- Any first relapse options that have not been tried

(2 new drugs;
triplet preferred)

Additional Options



- Belantamab mafodotin
- VDT-PACE like anthracycline containing regimens
- Selinexor
- Venetoclax (t11;14 only)
- Melphalan
- Bendamustine-based regimens
- Adding panobinostat
- Quadruplet regimens

Myeloma: Second or Higher Relapse

First Relapse Options



- Any first relapse options that have not been tried

(2 new drugs;
triplet preferred)

Isa-Pd, or DPd, or DKd, or KPd

Additional Options



- **Belamaf**
- VDT-PACE like anthracycline containing regimens
- Cyclo / benda / melphalan
- Panobinostat + PI
- Venetoclax [only t(11;14)]
- **Selinexor**
- **Melflufen**
- **CAR-T**
- **Bispecific**