

Algorithm of (cell) therapy indications in ALL for children

FRANCE



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« German-French day »

Phi- BCP ALL

1st line

Trial

CAALL F01
French trial

Future A2G
trial

HSCT indication (TBI ≥ 4y)

MRD TP1 ≥ 5x10⁻² (induction with anthracyclines)
OR MRD TP2 ≥ 10⁻³ (*Phi-like BCP ALL*: exposure of at least 14 d imatinib)
OR t(17;19)/TCF3-HLF

HR patients ≥ 16y (MRD1 ≥ 5%, or t(17;19), or MRD TP2 ≥ 10⁻⁴ and NCI HR)
OR MRD TP2 ≥ 5x10⁻⁴

CAR T Cells (tisa-cell) indication

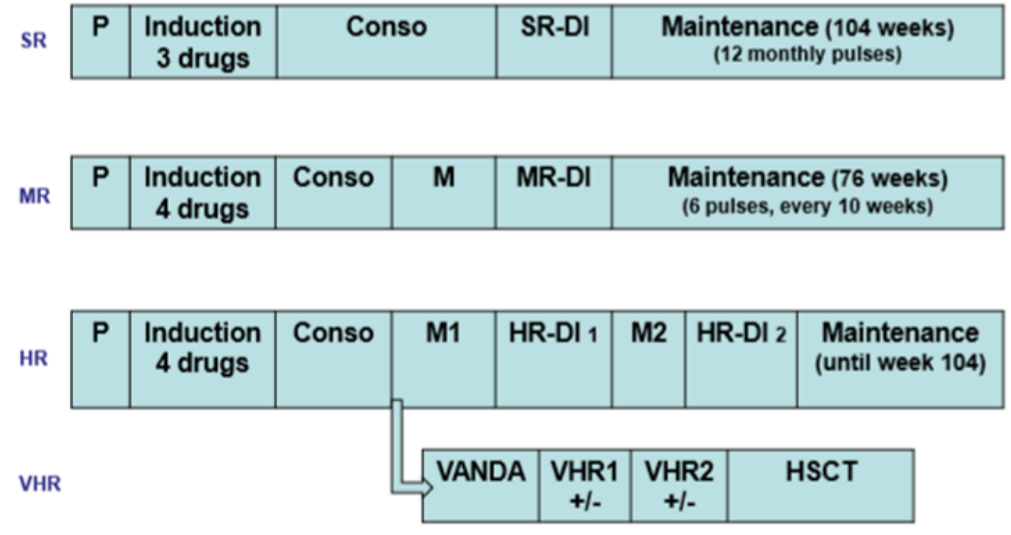
Refractory

CASSIOPEIA trial
 (NCI HR, MRD TP1 ≥ 1% AND MRD TP2 ≥ 10⁻⁴)

Investigational window for HR patients

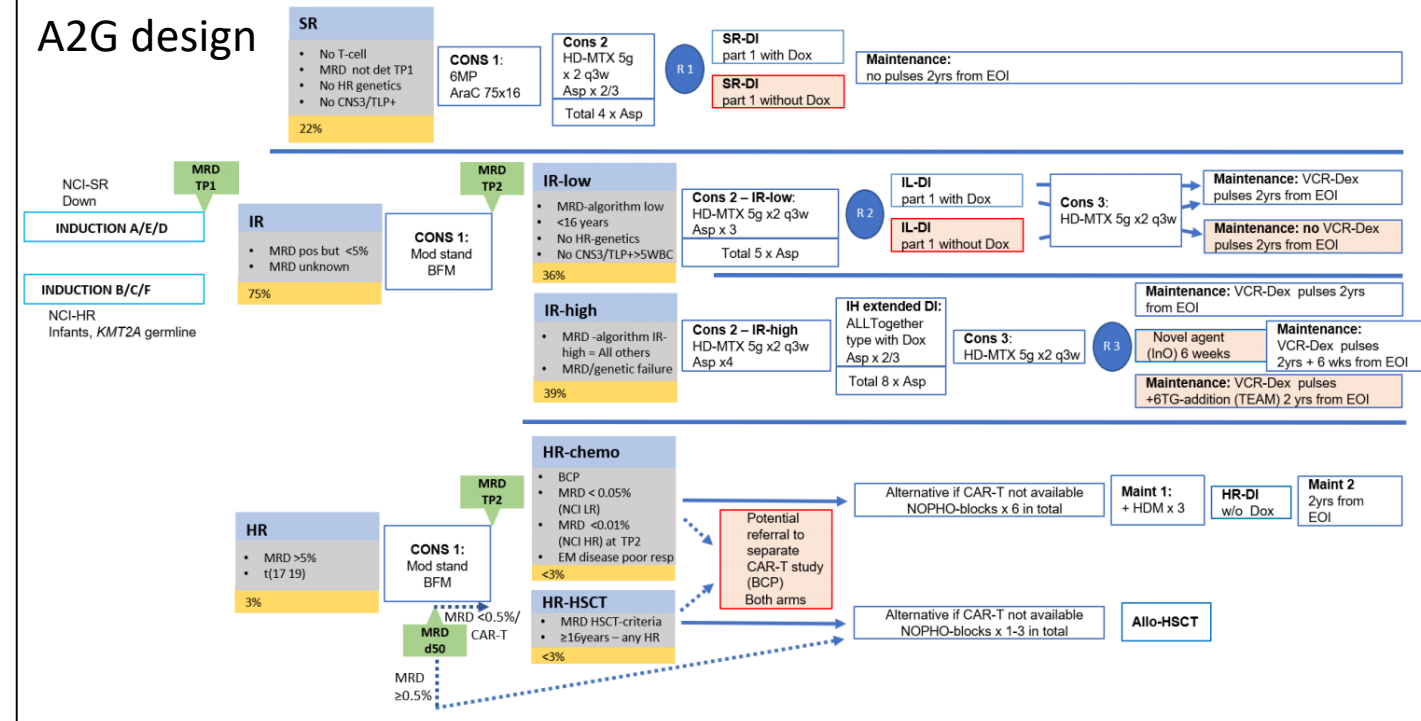
OVERVIEW

CAALL-F01: B-lineage ALL groups



P: Prednisone prephase; Conso: consolidation course
 DI: delayed intensification; M: high dose MTX cycles;
 HSCT: hematopoietic stem cell transplantation; VANDA/VHR1V/HR2: intensive courses pre HSCT

A2G design



Relapse

1st late medullary or extramedullary relapses

1st early / very early relapses

≥ 2nd relapse or relapse post HSCT

Trial

IntReALL SR

IntReALL HR
(future investigational inotuzumab)

Inotuzumab trial (ITCC 059)

HSCT indication (TBI ≥ 4y)

Day 28 MRD ≥ 10⁻³ (A arm) or 10⁻⁴ (B arm)

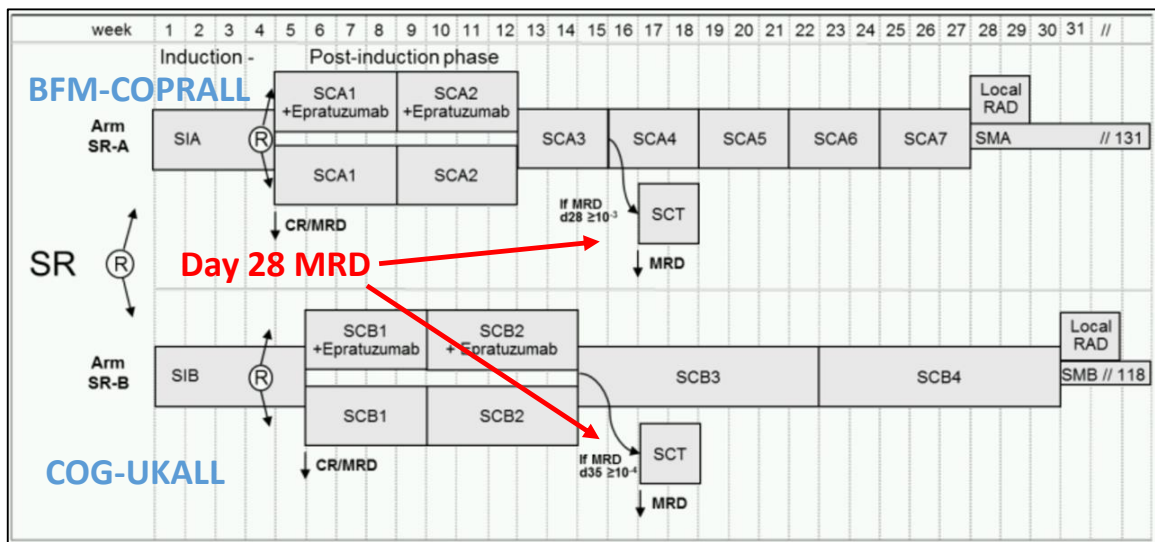
All patients w Blinatumomab preHSCT

If low MRD, if donor available, (if no previous HSCT)

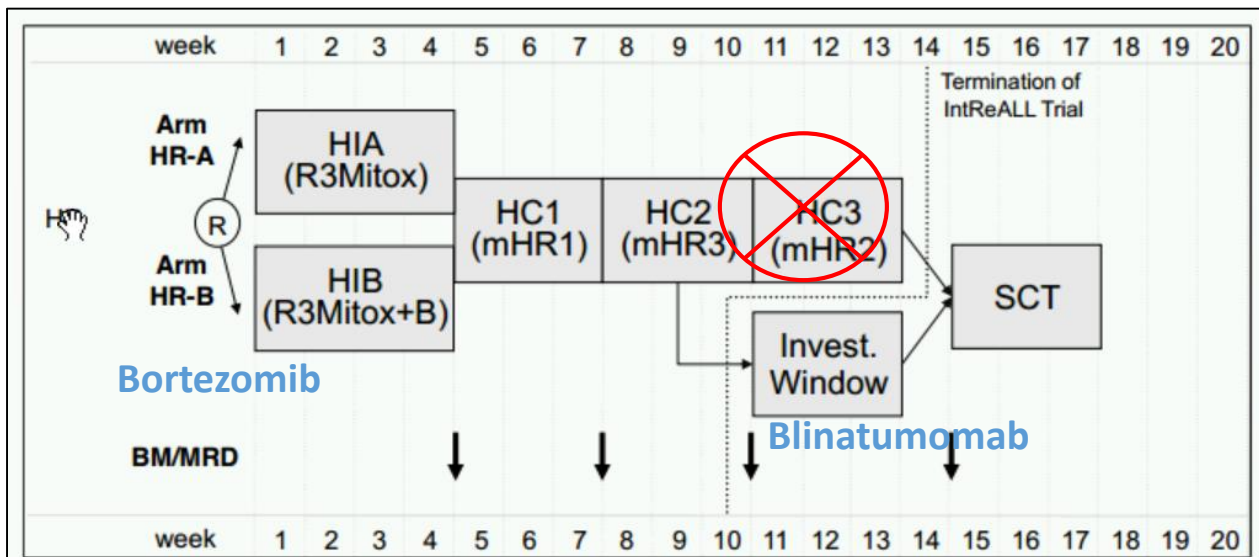
CAR T Cells (tisa-cell) indication

≥ 2 relapses
≥ 1 relapse post HSCT

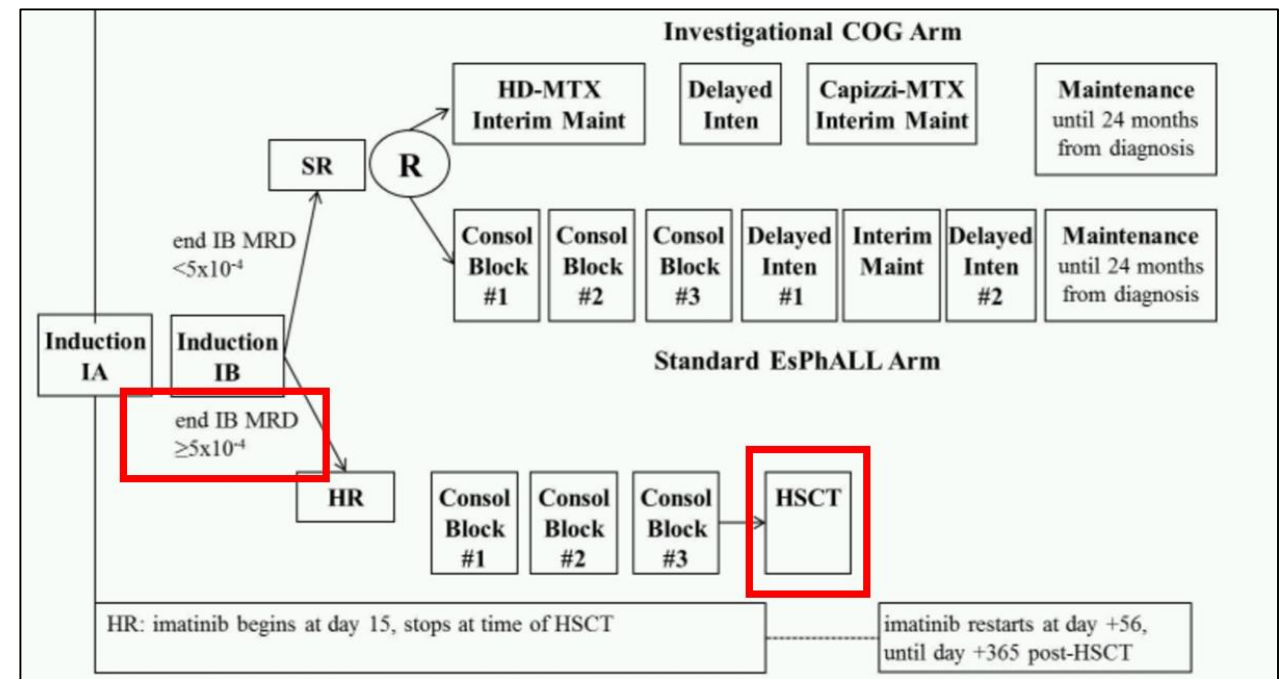
IntReALL SR



IntReALL HR



Phi+ BCP ALL



Trial

1st line

EsPhALL 02 (imatinib)

Relapse

TAKEDA trial (ponatinib, CT04501614)
OR NCT03934372 (ponatinib)

*Off protocol:
Pulses DXM + VCR + TKI, then
TKI + blinatumomab*

HSCT indication (TBI $\geq 4y$)

MRD (IgH-TCR) post IB $\geq 5 \times 10^{-4}$

All patients in CR (+TKI maintenance post HSCT)

CAR T Cells (tisa-cell) indication

Primary refractory patients

≥ 2 relapses
 ≥ 1 relapse post HSCT

Infant ALL

Trial

Interfant 21

1st line

Relapse

Off protocol:
Inotuzumab
Blinatumomab

HSCT indication
(T2B4F)

All HR patients
(WBC \geq 300 G/L or PPR
AND age < 6mths AND
MLL)
MR patients if MRD
TP1 \geq 1% OR MRD TP4
> 10⁻⁴

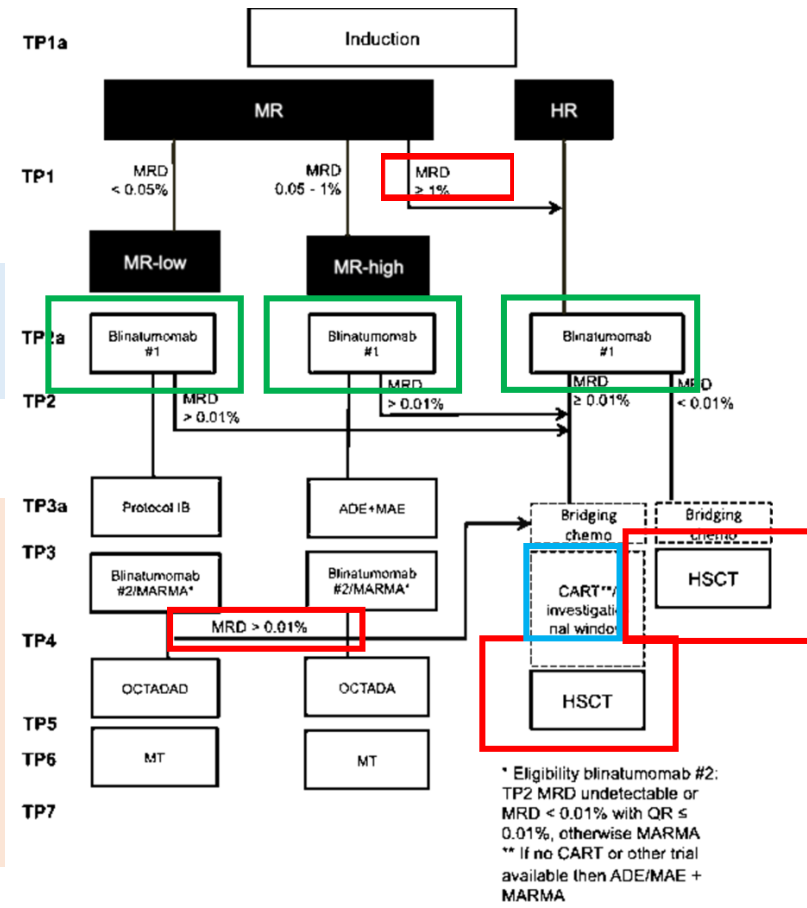
All patients in CR

CAR T Cells (tisa-cell)
indication

Investigational window
(bridge to HSCT) if MRD
TP2 \geq 10⁻⁴

Primary refractory
patients

\geq 2 relapses
 \geq 1 relapse post HSCT
...



T ALL

1st line

Relapse

All 1st relapses (except late EM)

Further relapses
Relapse post HSCT

Trial

CAALL F01
French trial

Future A2G
trial

IntReALL HR

*Off protocol:
Isatuximab? Carfilzomib?
Venetoclax?*

HSCT indication (12 Grays TBI ≥ 4y)

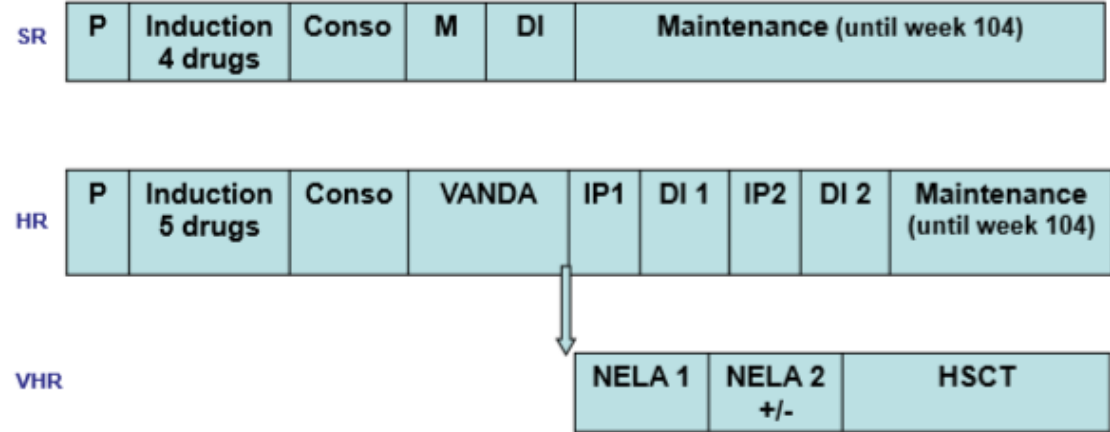
MRD TP1 ≥ 10⁻² AND day 8 PPR/OR MRD TP2 ≥ 10⁻³/OR MRD TP3 (post VANDA) ≥ 10⁻⁴

MRD TP1 ≥ 5% AND MRD TP2 ≥ 10⁻⁴/ OR MRD TP2 ≥ 5x 10⁻⁴/ OR MRD TP1 ≥ 5% and Age ≥16y

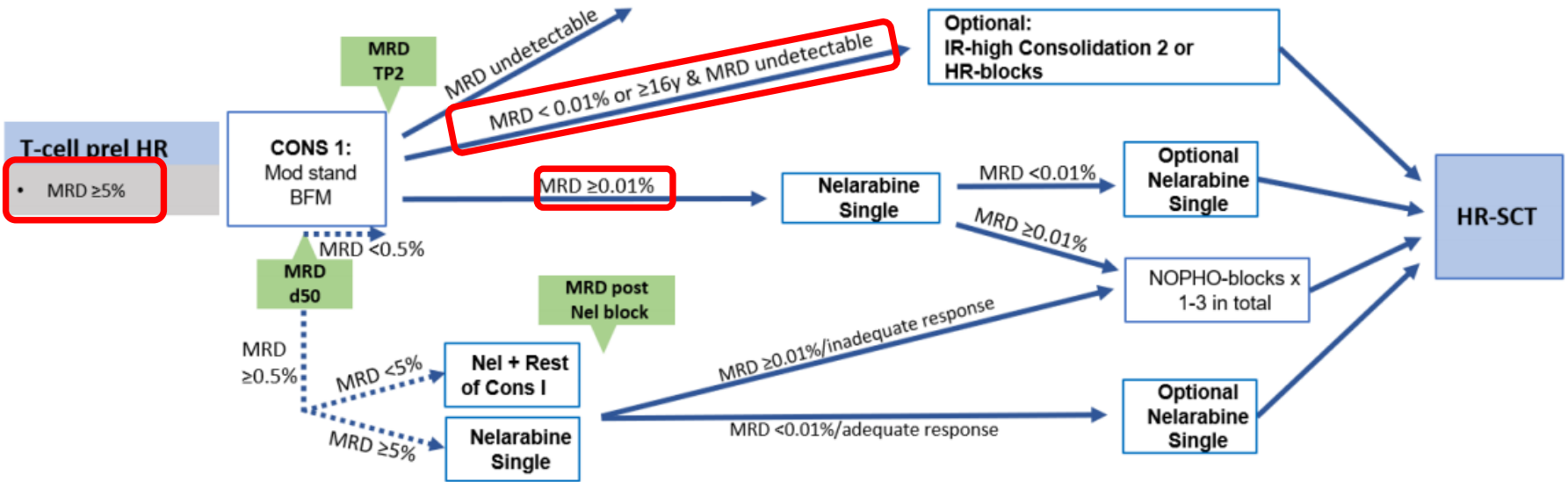
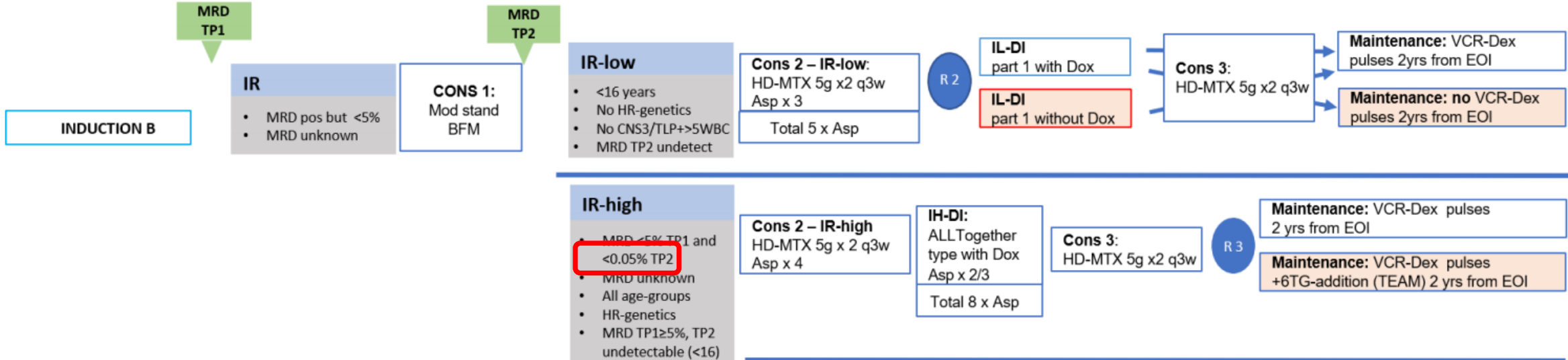
All patients

Anti CD7 ... CAR T cells?

CALL F01 (T ALL)



A2G (T ALL)



* Exception: HR-SCT MRD ≥5% EOI, MRD d 50 < 0.5%, TP2 not detectable MRD and <16y = IR-high