AALL 1731

Satellite Educational Training Module

JULY 2020

Presented to: Satellite Clinic Healthcare Providers
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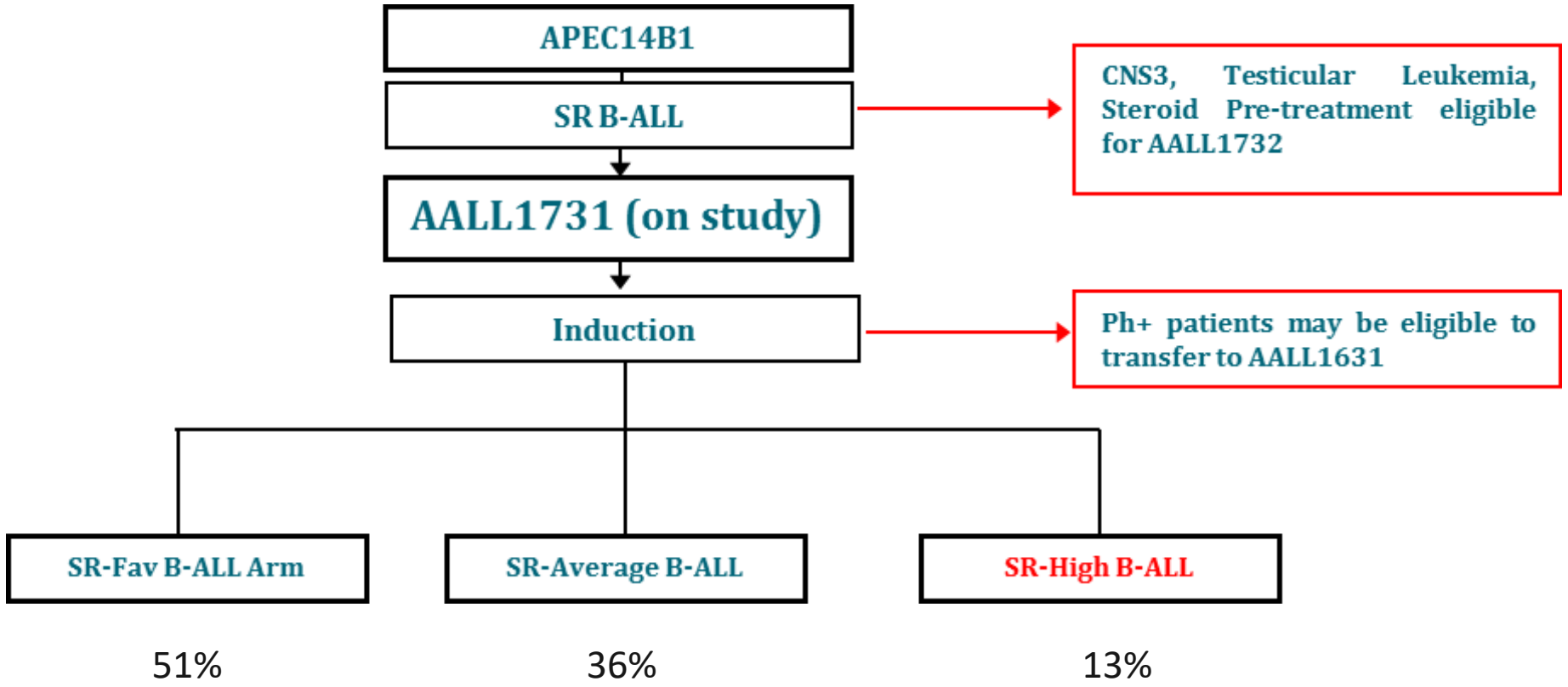
AALL 1731

- A Phase 3 Trial Investigating Blinatumomab (IND# 117467, NSC# 765986) in Combination with Chemotherapy in Patients with Newly Diagnosed Standard Risk or Down syndrome B-Lymphoblastic Leukemia (B-ALL) and the Treatment of Patients with Localized B-Lymphoblastic Lymphoma (B-LLy)

Principles behind AALL 1731

1. Can we identify additional subsets of NCI SR patients with outstanding outcomes by using new MRD measurement techniques?
2. Can we use immunotherapy to improve the outcomes of the remaining NCI SR patients (i.e. those with higher risk features?)
3. Patients who start off as NCI SR but are found to have higher risk features requiring intensified therapy will stay on 1731
4. Patients with Down Syndrome (DS) should have the same chance to benefit from novel immunotherapies as those without DS

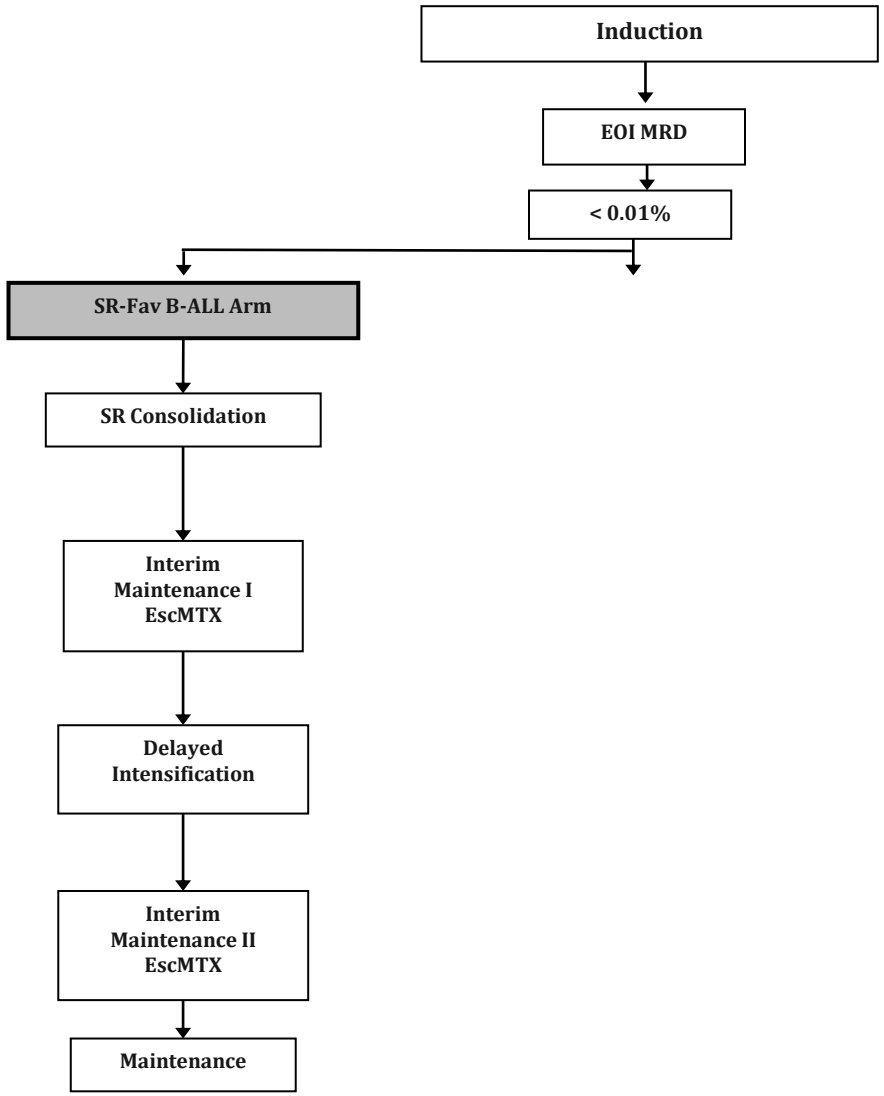
Risk Stratification of NCI SR B-ALL



SR-Favorable

- NCI SR
- CNS 1/2
- Favorable Cytogenetics (ETV6/RUNX1 or Double Trisomies (DT))
- D8 Peripheral Blood (PB) MRD <1%
- End of Induction (EOI) Bone Marrow MRD <0.01%

Patients receive standard therapy with a uniform duration of Maintenance therapy, regardless of sex.



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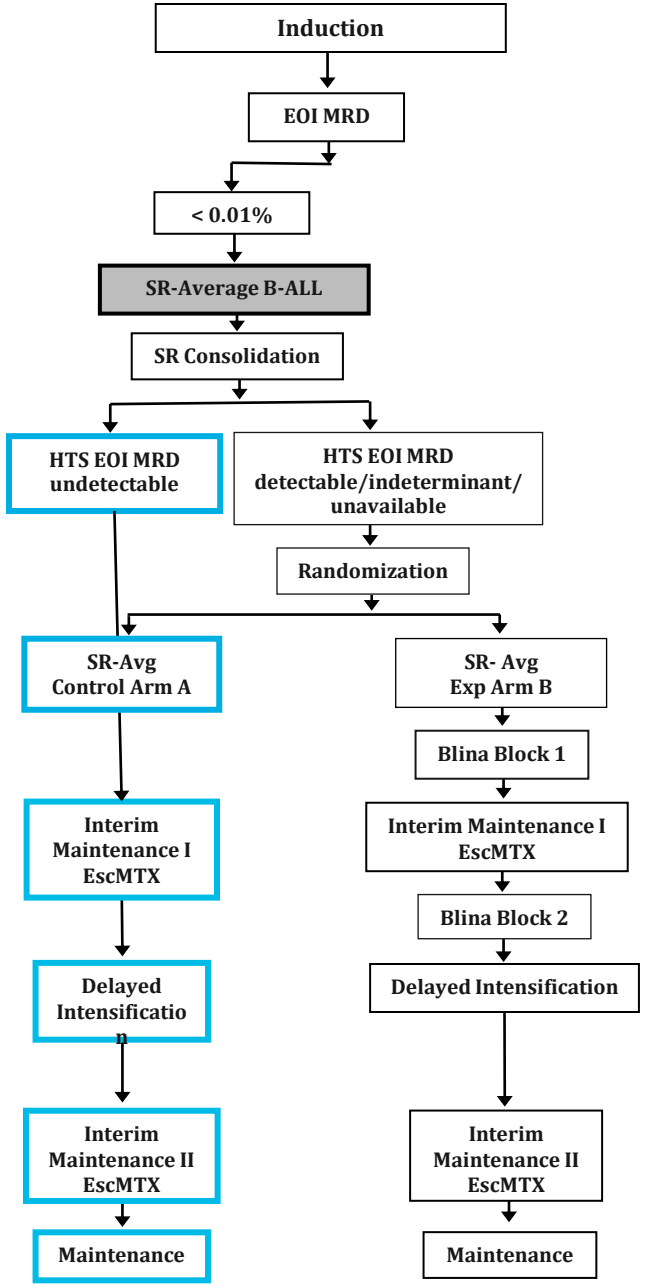
SR - Average

Patients with **undetectable MRD** as measured by flow cytometry and High Throughput Sequencing (HTS) at the EOI will receive standard therapy.



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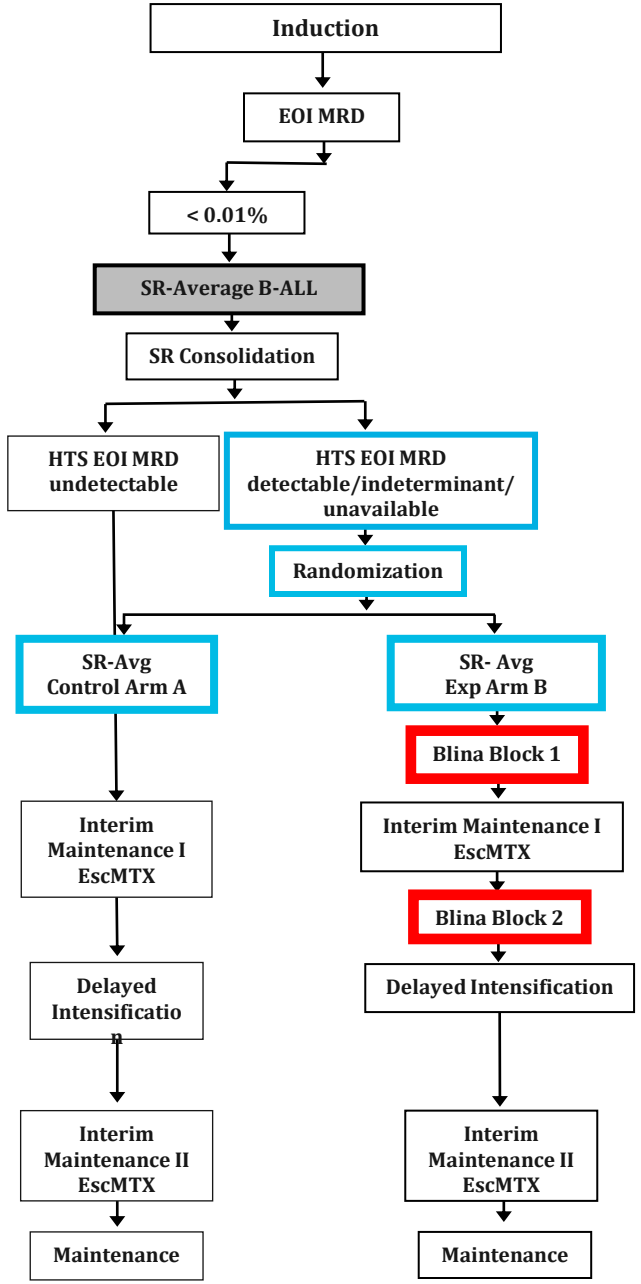
SR - Average

Patients with:

- MRD NEGATIVE by flow cytometry AND HTS EOI MRD positive, indeterminate, or unavailable
- Double Trisomies with EOI MRD positive

will be randomized to receive standard therapy (ARM A) or standard therapy plus 2 cycles of blinatumomab (ARM B)

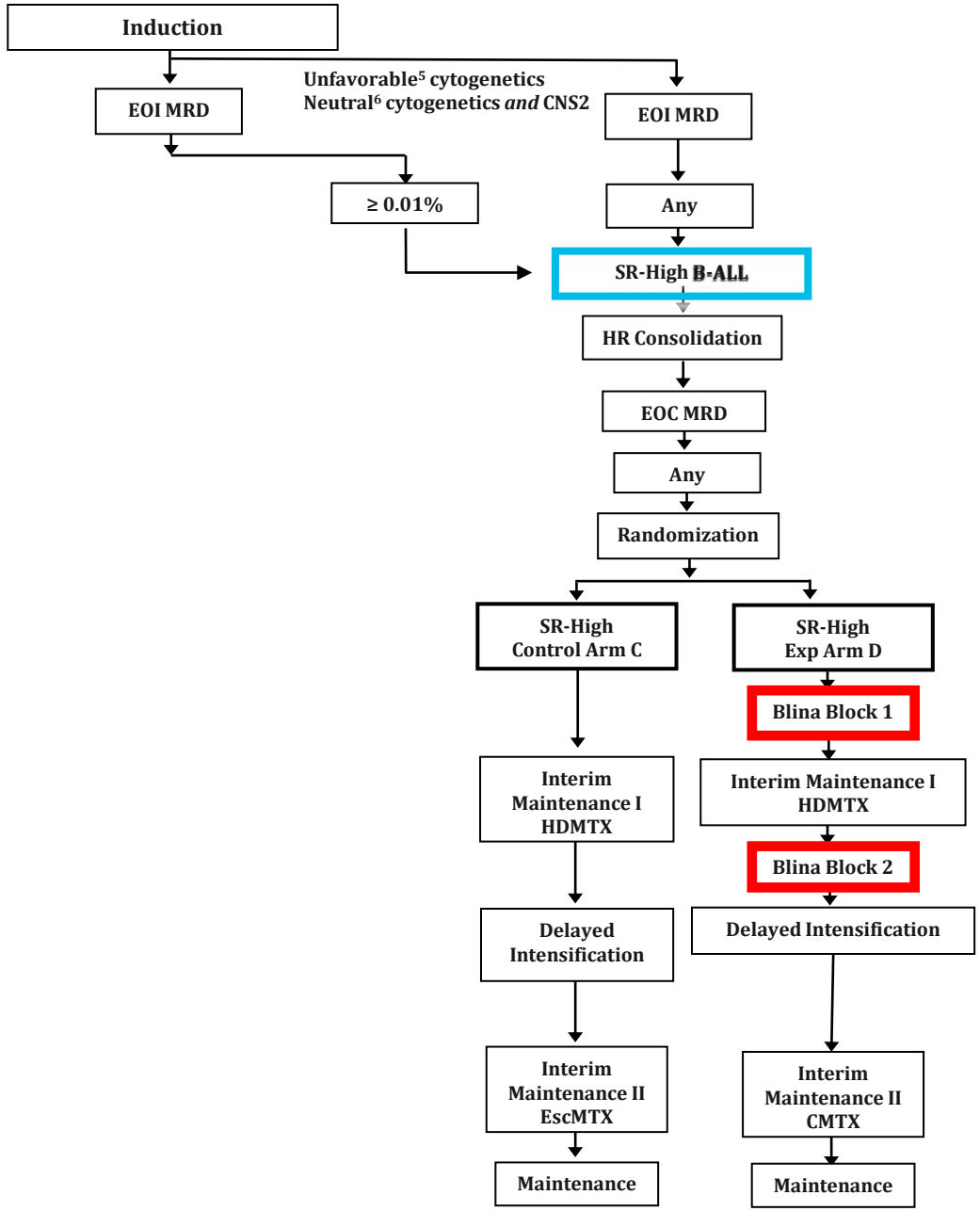


What is HTS MRD?

- Minimal residual disease (MRD) has been used for a decade to looks for small amounts of leukemia
- Patients who are MRD positive at the end of Induction have worse outcomes, but do better if you intensify treatment
- MRD currently measured by flow cytometry, which can detect down to 1/10,000 leukemia cells
- The new “High Throughput Sequencing” is much more sensitive and can detect to a level of 1/1,000,000
- Retrospective data shows that patients who are flow and HTS MRD negative at end of Induction have fantastic outcomes

SR - High

- Previously these patients were ‘off study’ or switched to HR protocol
- Includes End of Induction MRD by flow positive, Unfavorable cytogenetics, CNS2
- These patients will remain on study with HR therapy AND eligible for Blinatumomab randomization



Blinatumomab

- A bispecific single-chain antibody that targets CD19 antigen and redirects CD3+ T cells for the selective lysis of tumor cells
- Very short half life so administered as a 28 day continuous infusion
- Bags changed every 4-7 days at tertiary centre
- Admitted at the tertiary centres for the first 3 days of first cycle for monitoring, and 1-2 days of subsequent cycles Patients are generally very well during administration
- Main common serious adverse events in patients include:
  - Cytokine Release Syndrome (CRS)
  - Neurotoxicity (reversible in essentially all cases to date)

Duration of Maintenance in Boys

- The Children's Cancer Group (CCG) previously noted that boys with ALL did slightly worse than girls, so they extended their maintenance duration to 2.5 years

Trial Group	Length of therapy	Gender-based difference?
BFM-ALL 2000	24 months from diagnosis	No
St Jude Total XV	120 – 146 weeks*	Yes*
DFCI 00-01	104 weeks post CR	No
UK ALL 2003	2-3 years from beginning of Interim Maintenance	Yes
DCOG ALL-9	109 weeks	No
NOPHO ALL-2000	2-2.5 years post diagnosis	No

- On 1731, duration of maintenance therapy will be 2 years regardless of sex

What do I need to know at the satellite?

- All blinatumomab related administration and impacts will happen at the primary treatment centre, not satellites
- Blinatumomab cycles are in ADDITION to standard therapy, so all ‘regular’ chemo visits should continue
- High Risk patients STAY on study, Patients may be on a “standard risk” trial, but be getting intensified chemotherapy backbones (e.g. HD-MTX)
- ALL Down Syndrome Patients are included in this study
- Maintenance therapy duration is the same for both boys and girls
- As with all studies, clinical documentation and communication with satellite about any potential toxicities remains crucial

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