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Title of talk: Ma-Spore ALL studies: Truly Asia approach to Curing Childhood ALL

Abstract:

Despite its deceptively similar morphology under light microscopy, ALL is highly heterogeneous. Its heterogeneity is underlined by >20 distinct genetic drivers; each genetic driver conferring its own distinct risk of relapse. Whole genome transcriptomic sequencing using RNA-Seq can help define exactly each's patient genetic aberration that is driving his ALL. Increasingly study groups like St Jude Total 17 and Ma-Spore ALL 2020 study are using RNA-Seq to better define the genetic drivers and refine the risk stratification.

Low risk ALL is characterized by low risk of relapse. Features of low risk ALL include:

1. NCI standard risk – age 1-10 and WBC <50,000/uL at presentation.
2. Favorable genetics – Hyperdiploidy and ETV6-RUNX1
3. Rapid early response to therapy as defined by end of induction MRD <0.01%.
4. CNS 1 disease

There are considerable interactions between the first 3 low risk factors.

It is increasingly clear that further intensification of therapy does not improve outcome for low-risk ALL. COG AALL0331 study showed that children with ALL with all of the above low risk features (SR-low) did exceedingly well with 3-drug induction, mild consolidation and one block of COG Protocol II. Intensification with 4-additional doses of PEG-L-asp although marginally reduced the risk of relapse, did not improve overall outcome. UKALL 2003 SR arm showed that 2 blocks of delayed intensification Protocol II yielded similar outcome as one block.

As a result, many groups have started to reduce the intensity of therapy for low risk ALL. Ma-Spore ALL 2010 Standard Risk arm completely eliminated anthracyclines in low risk ALL patients, reducing toxicity without compromising outcomes. COG AALL0932 showed that in NCI SR ALL, 4 weekly dexa/vincristine pulse did not improve outcome compared to 12 weekly dexa/vincristine pulses.

In this talk, I will review some of the world's experience in managing low risk ALL and suggest that for this low risk group, giving less chemotherapy can actually achieve more.