MCL Breakout 1 Biology and Treatment Options Presenter: Robert Chen, MD, City of Hope

Critical to go for the longest good 1st remission

MRD: Requires initial tumor tissue and ongoing fresh blood samples. “No one is tracking MRD”, suggesting that there isn’t enough research on how to integrate MRD results into practice guidelines. He suggests using MRD only if participating in a clinical trial.

Treatment research: Ibrutinib (IBR) and Acalabrutinib must be taken continually as no studies have been done examining outcomes if either drug is stopped. BUT Dr. Chen then cited a case where Acalabrutinib “MIGHT” prolong remission even though it was stopped due to adverse effects “for several months” then back on for several months.

Bortenazamib was used post IBR failure, providing a 2 year remission. The remission increased to 4 years PFS if patient was in CR (vs PR) prior to starting IBR. And PFS of 33 months if given after 1st relapse vs waiting till after 2nd or 3rd relapse.

For anyone looking to post a direct link to the Bortenazamib study, the reference is Wang et al. Blood, 2016.

Venetoclax, a BCL2 inhibitor, is being studied as an option post IBR failure There is an IBR + Venetoclax+ Rituxan combo ongoing. https://clinicaltrials.gov/ct2/show/NCT03710772. The reason CAR-T is available only after IBR failure was how the CAR-T trials were approved.

Dr. Chen explains the lack of Acalabrutinib + Venetoclax trials resulting from administrative delays occurring in Pharma vs. Government or privately funded research.

MCL Breakout 2 Novel therapies and clinical trials Presenter: Sven DeVos, MD UCLA

Flow cytometry is an effective monitoring blood test and more available in community settings vs. MRD testing. Dr. DeVos’ opinion is that Rituxan Maintenance is proven only for 2 years, not longer. He further states that the best current treatment offering a long remission is auto SCT then Rituxan maintenance. (We heard other presenters suggesting 3 or more years of R maintenance post auto sct prolongs OS, confirming that there continues to be a lack of consensus on R maintenance.)

Research trends: Less toxic chemos in induction treatment (vs auto sct) are still providing 5+ years OS for people opting out of sct for any reason. That being said, the oldest sct patient at UCLA is 81 years old! Many current trials no longer have an upper age cut off but continue to limit participants to over 18 years old. Many trials are exploring combination therapies vs. studying new drugs since there is strong evidence that single agents provide a shorter remission. Combination therapies minimize resistance and “hit lymphoma and the immune system” from more/all angles, balancing the risk of increased toxicity of combination therapies. The BTK + BCL2 combination trials + CAR-T are most promising if toxicity can be safely managed.

Dr. DeVos believes that the most promising current trial he’s aware of combines IBR+ Venetoclax, and Obinamab.