



## **FCR v BR? Is one better?**

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### **TRANSCRIPT**

Now I'm going to talk about the choice in chemoimmunotherapy, FCR (fludarabine, cyclophosphamide and rituximab) vs BR. FCR has been our standard therapy for previously untreated fit patients with CLL under about the age of 70. BR (bendamustine and rituximab) is a relatively newer therapy which had been studied in a couple of phase II trials, smaller single arm trials, and looked rather promising.

For that reason, it was studied in a head-to-head trial against FCR in fact. This was the CLL10 study of the German CLL study group. They took fit patients of any age, as long as they had very good renal function and no major medical comorbidities, and they randomly assigned them to receive FCR vs BR. They found that FCR was better in terms of the likelihood of inducing complete remission where there is no detectable disease and the likelihood of making patients MRD negative where even with a very highly sensitive test we can't find any disease, which is likely the first step to cure. It was better in terms of the overall likelihood of how long the disease stayed away. However; there was no difference in the overall survival. In this particular study there was a bit more toxicity with the BR, which is in part because there was no planned use of supportive care measures like growth factors and antibiotic prophylaxis which are very commonly used in these regimens and I would certainly recommend that anyone who's getting FCR or BR get because it reduces the toxicity significantly.

In addition, we now have long-term follow-up data from three different studies showing that FCR results in possible cure in about half the patients, those who have mutated IGH without high risk cytogenetics. They have a 60% chance of long-term remission and at that time many have no detectable disease even with highly sensitive tests. There is absolutely

no evidence at all that BR has any potential to result in this possible cure because after BR there's continuous relapse.

For a person who is eligible for chemoimmunotherapy considering this treatment, FCR is preferred to BR, especially if they are under 65 and have no medical problems. In the trial that directly compared these chemo regimens head-to-head, in the patients over 65 some of the toxicity was worse in FCR compared to BR. Again, that was partly because they did not use antibody prophylaxis or growth factors, which would have helped.

With that being said, it could be reasonable to use BR, particularly in this older patient population, but it has to be recognized that you will be giving up in a potential for possible long-term cure with FCR. There is a fundamental distinction between these two chemotherapy regimens in that context. I would note, however, that over a certain age of about 70, the use of FCR can potentially be dangerous especially if the person has reduced renal function or bone marrow that has suffered prior insults. We can't always tell that ahead of time, so for patients over 70 it's generally not a good idea to consider FCR, unless your health is extremely good and laboratory tests indicate very good renal function. There is a small subset for whom it's safe, who meet the criteria of entry for that randomized trial, but otherwise, unfortunately, in general that regime probably should not be used in older patients and other options like BR or ibrutinib can potentially be considered.