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https://reachmd.com/programs/cme/balancing-act-immune-reconstitution-vs-immune-suppression/32227/

Released: 01/24/2025
Valid until: 01/24/2026
Time needed to complete: 1h 04m

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Balancing Act: Immune Reconstitution vs Immune Suppression

Announcer:
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Dr. Obeidat:
This is CME on ReachMD, and I am Dr. Ahmed Obeidat. Joining me today is Dr. Mark Freedman.

Mark, what is the difference between immune reconstitution versus immune suppression?

Dr. Freedman:
Yes, because this is an important element of the mechanisms of some of our high-efficacy therapies today, and it distinguishes the group of drugs that need to be given persistently in order to have its efficacy, because as soon as you presumably stop the drug, the disease will come back because the effects of the drug will no longer be on board.

The benefits of an immune reconstitution-type treatment is that most of the suppression is brief and up front, and then it produces a durable response on the disease, so you don't need to re-treat. And examples of each, for instance, would be the current use of B cell-depleting therapies. As far as we know, you have to maintain that, otherwise you lose efficacy. Whereas drugs like cladribine or, one that's become less in favor, alemtuzumab, these were given as an immune reconstitution treatment. Brief shots of the medication for a month or a few days and then repeated again in a second year and then nothing. And the return of the immune system is such that it is competent, so it can still protect the body, but is no longer attacking the central nervous system. And that really frees up people for many years, that they don't need to then be constantly under the influences of an immunosuppressive medication.

Dr. Obeidat:
Yeah, these are great points. So kind of when you talk to patients about the difference between immune suppression and immune reconstitution, you can describe maybe the risk early on for the immune reconstitution. There is an immune depletion early on that is followed by this repopulation or reconstitution of the immune system, versus the immune suppression where there is always kind of going to be some sort of immune suppression. And one of the questions, you mentioned B cell-depleting therapies, but maybe in the future this could be a way of also using them by doing personalized type of therapy and following certain biomarkers for redosing versus dosing everyone on the same interval. That may help with some of the risks that can be associated with that group.

Dr. Freedman:
I think the real benefit is, is the brief exposure to the immunosuppression really reduces the kind of safety issues that would come with long-term immunosuppression. And if somebody is very concerned about that, then an immune reconstitution treatment lends itself to it. The other kind of interesting patient that might be ideal for this approach would be, say, a young woman who's got a more aggressive disease, warrants high-efficacy treatment, but is planning a family and doesn't want to have to go through the, well, I started and then stopped, and then the risk of return of disease during pregnancy. Maybe an immune reconstitution treatment for that individual, and then

they can – like, for instance with cladribine, you can start getting pregnant 18 months after starting the disease treatment and then, if it's worked properly and you have a durable response for a couple years, that'll sail you through your pregnancy without a problem. You don't have be exposed to any drugs and protect you for a period thereafter. So that would be an ideal kind of situation.

Or if you're dealing with somebody who may be immunocompromised because of comorbidities, because not everybody's perfect like they do in their clinical trials, an older individual, maybe with a number of comorbidities, a little bit more high-activity disease, you don't want to expose them long term because the older people are the ones who get all the problems. Right? So you could then use an immune reconstitution treatment approach for those individuals, where you limit the amount of time that they're suppressed and, therefore, underexposure for safety issues.

Dr. Obeidat:
Yeah. And we know also, there are some other implications for vaccine responses and other things that could be also taken into consideration.

Well, this has been a brief but really great discussion. Our time is up. Thank you for listening.

Dr. Freedman:
Thank you, Ahmed.

Announcer:
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