

## Monitoring for Treatment Side Effects

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### **Januario Castro, MD**

Associate Professor of Medicine, Division of Bone Marrow and Stem Cell Transplant  
UC San Diego Moores Cancer Center

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### **Andrew Schorr:**

Dr. Castro, we're still monitoring for side effects, right? Even with these new agents, you have to be careful and even as Dr. Keating said is we're now doing new things and we don't know the long-term result yet, right?

### **Dr. Castro:**

Exactly, and that is a learning curve. So, yes, with chemotherapy is, everybody's very familiar with those side effects. Unfortunately, when you give chemotherapy, you're not only killing the cancer cells, but you're destroying also the good cells that are kind of growing rapidly in the body.

The hair follicles, the lining of the, of the gastro-intestinal system, the skin cells, the cells that they're leave in the bone marrow improves the normal cells, so you see an array of side effects and toxicities that for the most part are very similar from one medication to the next to the next.

The next generation of treatment, the ones that you see listed in here, even though hypothetically and biologically have been designed to be extremely specific, again, following that analogy of the train station to go just to one particular area of that train station and not to interfere with other kind of parts of the system, it is extremely complicated.

How the cell is working around those pathways, and, in general, there are overlapping elements that belong to one or another pathway. So what happens is there are side effects that can appear even though the medications are designed to be extremely effective or specific.

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One of the problems that we need to kind of be aware of, and Dr. Keating was mentioning this, is that it is unknown what is going to happen, one, in the long term, when you take one, two, three years of these medications, what is going to happen.

Fortunately, what is known until now is that it appears to be that for a long-term administration, there doesn't appear to be causing any unexpected or new side effects or toxicities. Second is, are those cells changing biologically. You keep them under some sort of suppression, but they are not disappearing.

It's possible that that kind of biological suppressions are going to make them more resilient to future treatments, or they're going to make them change biologically or genetically.

And there are some concerns about the emergence of what is called the Richter's transformation, which is a different type of disease in which the cells just kind of change dramatically their phenotype and genotype, and they start behaving more aggressively.

And number three is just a combination of one plus two is not going to be just, say, as simple as just thinking or predicting from the side effects of each one of those individual drugs is going to be a potential challenge to kind of when you mix them together to see new toxicities.

And one of the examples is what Dr. Keating mentioned about some patients having lung toxicities and other kinds of unexpected side effects from the combination of two pills. So in the future, the clinical trials definitely they need to pay a lot of attention to this, and that's part of the challenge of when you design potential new strategies.

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