PHILIPPE GABRIEL STEG: PCSK9 inhibitors have a remarkable benefit risk profile. Given that benefit risk profile, we would love to use them in everybody. Unfortunately, because of their cost, that's not possible. At least it's not possible for the time being. It may change in the future, as the cost of these agents and these classes go down. But for the time being, we have to select where to start.

And clearly, we want to use these agents in the highest risk patients. Because if you start off with the highest risk, this is where you're going to get, literally, your greater bang for your buck. So who are the highest risk patients?

Well, there are a number of features that allow us to easily identify these patients. These are either clinical or biologic. The clinical features we know. Extensive severe coronary artery disease, polyvascular disease, particularly the presence of peripheral artery disease in conjunction with coronary artery disease, diabetes, repeated acute coronary syndromes, what I call frequent flyers.

We all know these patients who come back to the cath lab every six months, every year, because they have new events. These patients are extremely high risk. So these are clinical features that can easily identify patient profiles that might derive benefit.

Biological features, I would identify at least two. The first one is obviously LDL. The higher your baseline LDL, the higher your baseline risk. And since this is a class of drugs that will potently reduce LDL, we would like to use them in patients who start off with the highest baseline value to start with. And this is what consensus guidelines on both sides of the Atlantic have generally recommended.

For instance, the European Society of Cardiology in the EAS have put out a consensus guideline-- not a guideline, a consensus document-- last year which actually recommended that in secondary prevention, the highest risk patients be treated as soon as their LDL cholesterol is equal to or above 100 milligrams deciliter of LDL cholesterol with a PCSK9 inhibitor.

The last biological feature that seems to be associated with very high-risk and possibly specific benefit from PCSK9 inhibitors are patients with very elevated Lp (a) little a who we know have a higher risk and who appear to derive LDL cholesterol independent additional benefits from PCSK9 inhibitors, as we found in ODYSSEY outcomes.