We have proof of concept for CAR-NK and we also know that the first patient was dosed with CAR Macrophage trial earlier this year. From CAR-T moving into CAR-NK moving into CAR Macrophage, how does that compare, what is the benefits, the thoughts around moving into CAR-NK, moving into car macrophage, versus where we are with CAR-T?

Mike Nicholson: So I'll start with the CAR Macrophage approach just because its I feel like CAR-NK is certainly not CAR-T but perhaps a little bit closer than a CAR M. I'm personally very excited about CAR Macrophage just because I feel like it allows us to ask an entirely different set of questions because it works fundamentally from a very different mechanism. The idea of still using a CAR or some sort of targeting molecule to specify the engulfment you might get from an engineered macrophage, and of course there are a couple of reasons to do this. Number one if you can specifically target your macrophages to engulf specific tumor types that's good but then we also expect that we'll see antigen presentation and then activation of the immune system, it's almost an amplification signal. I was talking to Chris at one point and it's kind of like combining a CAR-T with a vaccine strategy almost, a cancer vaccine. So, I think on the one hand, what a great approach, because we can potentially attack tumors from two angles on the other side, that now doubles the complexity because we have several things we are trying to model and understand. Not to mention we still, as much as we understand how CARs work and CAR-Ts and to a lesser degree CAR-NKs. I think it's very exciting just because it is such a different effector cell to use, and opens up some mechanistic questions we can't address with CAR-T. But it also is just full of more complexities, but I'm very excited to see what happens in this first trial and follow ups.

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Mark Gilbert: Maybe to talk a little bit about CAR-NK, while there aren't pivotal studies that are under way yet, I think work out of Anderson with Dr. Rezvani has demonstrated that you can produce and deliver CAR modified NK cells from cured blood and get these responses with an allogeneic cell product that's NK that mirror the effectiveness of currently approved CAR-T products. I think that there are a number of big questions out there right now, one that is we tend to treat the NK field as if it's all one cell and I don't believe that that is necessarily the case. Obviously, we have some companies that are working on classical NK cells, they aren't defined memory NK cells, NK T-Cells, and then gamma delta T-Cells, there are some similarities between those classes, and we tend to lump them all together, but it may be more of a continuum then a distinguishable strong difference between them. But it is possible to modify them, what signals we give a NK cell, because classical CAR construct are giving T-Cell signals to NK cells, and that appears to work but we haven't yet characterized what is the actual phenotype as those cells move forward and have we actually altered them in some specific way once they get in the body.

…So, I do think that CAR-NK is an approach, I think that there are some real technical hurdles in using true NK cells because of the freeze thaw sensitivity of those cells that may be challenging for that field. But it really is an interesting approach in using these other cell types within the field and they seem to match up with CAR-T, at least in homological malignancies, whether there are differences in solid tumor the jury's still out.

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Christopher Heery: I would just emphasize that one point about CAR Macrophage, what is really interesting about that idea is the ability for antigen cascade, and multi specific antigen response. I think when we look at the question of when we will see a breakthrough in solid tumors, one of the first questions is how do we account for the heterogeneity of expression in solid tumors. So, that does offer a really interesting opportunity to help account for that problem. I think there's a lot of learning that would have to happen there to get it just right, but I think it's a really compelling idea to be able to generate a multi specific immune response while also breaking down the tumor size initially with a highly effective other cell therapy, or maybe with that cell therapy product inserted directly into that tumor for instance. Just one other comment on marks comments on CAR-NK we should not also forget that there's also generic activated NKs and those are also intended to help solve this problem of multi specific mini tumor antigens, its actually the problem that Arcellx is trying to work on. Could we take one universal CAR-T cell with mini potential target tags, and I think the highly activated NK cells we're actually seeing some interesting responses with those in combination with already known IGG1 monoclonal antibodies, so I think that's also a really interesting field. But it certainly suggests that NK cells are efficient killers, and they certainly could be just as good, but again it took 20+ years for car t cells to get to where they are today, and I think we should expect that any new cell product or new approach is going to take a while for us to get it totally right, but it is exciting to see that there are these opportunities out there.