Array BioPharma Inc.(Gastrointestinal Cancer BEACON CRC)
June 23, 2018

Corporate Speakers

- Ron Squarer; Array BioPharma Inc.; CEO and Director
- Axel Grothey; Mayo Clinic; Chair, Division of Hematology/Oncology, Department of Internal Medicine
- Victor Sandor; Array BioPharma Inc.; Chief Medical Officer

Participants

- Chris Shibutani; Cowen and Company, LLC; Analyst
- Anupam Rama; JP Morgan Chase & Co; Analyst
- Stephen Willey; Stifel, Nicolaus & Company, Incorporated; Analyst

PRESENTATION

Operator^ Good day, ladies and gentlemen, and welcome to the Encore Webcast of the ESMO 20th World Congress on Gastrointestinal Cancer BEACON CRC Safety Lead-In. (Operator Instructions) As a reminder, this conference may be recorded.

I would now like to turn the conference over to Mr. Ron Squarer, Chief Executive Officer. Sir, you may begin.

Ron Squarer^ Well, good morning and good afternoon, depending on where people are today, for those who are joining us. This is Ron Squarer, CEO of Array BioPharma. I like to thank everyone for joining this ENCORE webcast of our ESMO BEACON CRC presentation.

I'm joined today by our Chief Medical Officer, Dr. Victor Sandor; and Dr. Axel Grothey, former consultant and professor in the Division of Hematology/Oncology at the Mayo Clinic, soon to be moving to a new position at the West Clinic at the University of Tennessee. Dr. Grothey will be presenting the overall survival results from our Phase 3 BEACON CRC trial that were presented just earlier today.

And as a reminder, we are going to be making forward-looking statements and I'd encourage all investors to take a look at our recent 10-Qs and 10-Ks and other recent SEC filings for a full description of risk associated with forecasts and predictions that we'll be making today.

We only have a limited amount of time for questions at the end of the call. And with that, I'm very pleased to turn the call now over to Dr. Grothey.

Axel Grothey^ Thank you, Ron, and thanks for everyone joining the call. This will be a recapping of kind of the presentation that Eric Van Cutsem from Belgium presented

today as an oral presentation at the World GI meeting here in Barcelona, beautiful Barcelona, and it's the BEACON CRC study safety lead-in, assessment of the BRAF inhibitor, encorafenib, plus the MEK inhibitor, binimetinib, anti-EGF receptor inhibitor antibody cetuximab for BRAFV600E metastatic colorectal cancer.

So BRAFV600E mutated colorectal cancer is a cancer with an unmet need. About 10% to 15% of patients with colorectal cancer carry this mutation. And in particular in the metastatic setting, it has a very poor prognosis, again constitutes an unmet need.

There's really no established standard of care. We all use chemotherapy in first-line, but median overall survival in the second-line setting is between 4 to 6 months, progression-free survival very short, very low response rate with conventional therapy.

There's some preliminary data from the randomized intergroup study from the United States, the SWOG 1406 study, now on Slide 4 where I am, which combined an all first generation BRAF inhibitor with standard irinotecan and chemotherapy and an anti-EGF receptor inhibitor and it showed an improvement compared to what we normally did for the irinotecan and cetuximab, but clearly not a home run yet in terms of improvement in overall survival and progression-free survival.

The problem that we see with the BRAF mutated cancers -- I mean, we have BRAF inhibitors that work quite well in melanoma and in thyroid cancer, where we see the same mutation, but in colorectal cancer the situation is more complicated and we actually see feedback loop activation of this MAP kinases pathway which is very pivotal for the biology of colorectal cancer. So that we really need to use our biologic understanding of inhibition of this pathway to really make a difference for patients.

So there are preliminary data with the [Array] compounds, encorafenib plus cetuximab, which actually had intriguing results even without the use of chemotherapy, with median overall survival of 9.3 months and progression-free survival of 4 months and some substantial response rate in this unmet need patient population of 24%, which led to the idea of "can we use a BRAF inhibitor plus a MEK inhibitor and an anti-EGF receptor inhibitor and make it more efficacious."

So in slide 5 here, you see some preclinical data of a triplet combination just using biologics, a BRAF inhibitor, a MEK inhibitor, anti-EGF receptor inhibitor to really shut down this pathway, which is a pivotal pathway for tumor biology in BRAF mutant colorectal cancer. So there's a pretty good preclinical and biologic rational.

So the BEACON study is a Phase 3 study which will investigate or is investigating, currently is actively enrolling patients with this triplet therapy of the combination that I mentioned, the doublet treatment of the BRAF inhibitor encorafenib plus cetuximab and the control arm of FOLFIRI-cetuximab or irinotecan-cetuximab, which I think in spite of the fact that we know it's not great, highly efficacious, is from a regulatory perspective the established control worldwide, in the United States, in Japan and in Europe.

Now, in order to make this -- to lead into this trial, we had to run a safety lead-in phase to establish the safety of the combination of encorafenib, binimetinib and cetuximab. And this is exactly what we are looking at right now, 30-patient population as a safety lead-in. And we didn't only look at safety, but also efficacy and this is kind of the highlight of this conference here.

So the safety lead-in had 2 components, a dose determining cohort, 9 patients, and the dose expansion cohort we're looking at these 30 patients which were presented here with a triplet combination.

On Slide 7, you see the eligibility criteria. So with BRAFV600E mutant tumors, progress after 1 or 2 prior lines of therapy, good performance status. And prior treatment with irinotecan was allowed, keeping in mind that in the eventual BEACON study irinotecan actually serves as one of the control arm. So this is the cohort that we are looking at.

On Slide 8, you see baseline patient characteristics. Interestingly, one patient who was included in the safety lead-in phase did not have a BRAFV600E mutation, so he was excluded from the analysis -- from the efficacy analysis because non-V600E mutant tumors cannot benefit from this combination.

Otherwise it's kind of a spread of patients like we would expect, more right sided tumors because we know that BRAF mutations are more common in right sided tumors, but 50:50 split between 1 or 2 lines of prior therapy and only one patient had an MSI high cancer or remiss or repetition cancer, because we know there're some overlap in about 10%, 15% of patients or 15%, 20% of patients with BRAF mutation that have MSI high morphology. So this is a pretty kind of commonly seen patient population for BRAFV600E mutant tumors.

So on Slide 9, you see the patient disposition. So of the 30 patients who entered the study, 30 were evaluated for safety, 29 for efficacy, again eliminating this one patient who did not have a BRAFV600E mutant tumor. 80% of patients, 24, have now discontinued therapy, most of them for progressive disease. At some point, of course, these tumors progressed. Only one patient had unacceptable AEs and failed to tolerate the study drug and 6 patients are still on treatment in this setting.

Now, the next slide, Slide 10, shows the best overall response. And keep in mind that responses in this patient population is extremely rare and normally not durable. So looking at a response rate here of 48%, including 3 complete responders, it's quite remarkable. And when I look at the patient breakdown between the patients who had 1 or 2 prior lines of therapy, 62% response rate for patients who were kind of in the second line setting, 31% of patients who were in a third line setting, that is quite impressive. Median duration of response, 5.5 months, again on the higher end of what we would ever expect, and 43% of responders had a duration of response over 6 months.

So in Slide 11, you see waterfall plot, which is again quite remarkable. By definition there's not a single patient who actually had progression of disease. And you can see

except for one bar, all these bars go down, meaning, indicating some form of tumor shrinkage.

And this is even more impressive when you kind of superimpose the data of the SWOG study that I mentioned with the control arm of the SWOG study -- actually, the control arm of the BEACON study. This is what we can expect from the control arm of the Phase 3 study. You can see the waterfall plot looks very different. I also want to highlight, as you can see on this superimposed waterfall plot, that progression of tumors with BRAFV600E mutations is quite rapid normally. You can see that the doubling of tumor size indicated by 100% progression quite remarkably in most of these cancers that were in the control arm of the study.

When you look at on Slide 13, duration of response and duration of exposure, you can see on the swimmers plot the arrows indicate patients who are still on treatment and the stars indicate when patients had first response. Again, all these data that we see are very favorable compared to historic controls and everything that we know about BRAFV600E mutant tumors. Median duration of exposure of agents, 7.9 months, also speaks to the tolerability of the regimen.

Now, on Slide 14, you see progression-free survival. Keep in mind that normally overall survival is less than 8 months and we see median progression-free survival here of 8 months, a curve that is again something we normally have not seen in this 29 patient population.

And when we break it down on Slide 15 by prior lines of regimen, whether the patients are in the second or third line of setting, now these breaks of course down to smaller patient population. There doesn't seem to be a big difference or any discernible difference at this point whether patients were treated in the second or in the third line setting, median progression-free survival of 8 months for both lines of therapy.

On Slide 16 are the overall survival data. These were clearly new data that had never been presented here. And data fully mature through 12.6 months. And at this point in time, as you can see, median overall survival is not reached. This is kind of approaching twice as long, the overall survival, of what we normally expect for patients in the second and third line setting with BRAFV600E mutant tumors. When you now look at the kind of survival rate at 6 months and at 12 months, in particular the 12 months survival rate of 60-plus percent in the second or third line setting, it's quite impressive.

So the next slide, Slide 18, talks about summary of safety events. Virtually every patient had some form of AEs, but only 70% of patients had grade 3/4 adverse events. And I'll break it down a little bit later. Reassuringly, only a few patients, 6 patients, had AEs leading to treatment discontinuation or 5 patients' AEs leading to dose interruption or interruption or dose changes. On-treatment deaths due to progression of disease, 5 patients, 17%.

Now, breaking it down in terms of AE management, AEs on Slide 19, And I would like to focus on the grade 3/4. Most of these AEs were in single, low single digits. The ones that went -- approach or went above 10% were fatigue, dyspnea and anemia, keeping in mind that these are patients who are in the second and third line setting.

When I compare this from my experience with standard chemotherapy, this actually compares very favorably to what we normally expect in patients treated with chemotherapy. This is better tolerable than what we normally expect from aggressive treatments like FOLFOX, FOLFIRI or FOLFOXIRI, triplet chemotherapy plus a biologic.

So when we conclude and summarize everything we've seen with what Eric Van Cutsem presented today, when you compare to historical data and this safety lead-in set, 29 patients with efficacy results, every parameter, whether it's response rate, progression-free survival or overall survival, does compare favorably with chemotherapy data, standard of care, but also over the results that we've seen with Encorafenib plus Cetuximab. So there seems to be the idea that a triplet could be superior to the doublets of a BRAF inhibitor plus an anti-EGF receptor inhibitor. But again the Phase 3 study we'll actually try to show exactly that.

The new data, I think the highlight of the presentation was that when we have fully mature data with a follow-up of 12.6 months, median overall survival in this normally very aggressive patient population, aggressive tumor was not reached; with an overall survival -- 1 year overall survival rate of 62%; median PFS, 8 months beyond what we normally expect for overall survival; unprecedented response rate, which are longer lasting; no unexpected toxicities.

And I'm pretty excited to be part of a team that is looking at the BEACON Phase 3 study in form of a steering committee. I think this has a great potential to really become a new standard of care in this setting.

So this safety lead-in will generate a lot of attention, whilst discussed by discussants, and again everyone I talked to and the reaction in the room was quite favorable when the data were presented.

With that, I'll close and I'll hand it over to Ron again.

Ron Squarer^ Yes. Thank you, Dr. Grothey. We are indeed very excited about these results. And as I mentioned, we have a short period of time available for questions. And so if we can turn it over to the operator for the first question please.

QUESTIONS AND ANSWERS

Operator^ (Operator Instructions) And your first question will come from the line of Chris Shibutani with Cowen.

Chris Shibutani^ Congratulations on the data, very impressive. And Dr. Grothey, I appreciate your comments there. It certainly seems as if with the patients that you're seeing this kind of impressive result, the number of lines of therapy do matter. I think investors are very keen to see what kind of potential plan you can envision if you were to move into earlier lines of therapy, perhaps in first line, perhaps is the question both for the company to comment upon as far as where your status is? And then, Dr. Grothey, comment about how you see the scenario for managing patients in that first line setting and the potential for this regimen?

Victor Sandor^ Hi, Chris. It's Victor here. I'm going to start and then I'll let Dr. Grothey chime in with his views. I think as a company in terms of taking it forward into first line, obviously we're very excited by the prospect of doing that. And I think that the data that we're showing both in terms of the response rate for the second line patients at 62% and then just the strength of the data overall would suggest that this could be of great value in the first line setting.

So in terms of what that looks like, we're still working that out from a regulatory point of view. But there are a number of different options that range from doing sort of small randomized studies to even potentially looking at trying to show a good response rate that's durable in a single-arm study. So, Dr. Grothey?

Axel Grothey^ I mean, I echo to what you say. The question is very well taken. I mean, this is -- this really screams for it being used in an earlier line setting. When you look at the excitement around this data and particularly since this is not even -- this is exploring -- exploiting biology [mix] -- using our biologic understanding of pathway management and pathway inhibition. We don't even need chemotherapy. This is really targeting the underlying oncogene mechanism of this cancer, so it really screams for a first line treatment. And I know we have discussions about how to best document the efficacy in a convincing manner that this might actually also convince regulatory agencies at some point. So I'm pretty much -- I'm very excited about being part of this effort and I can see a lot potential for first line treatment here.

Operator^ And the next question will come from the line of Anupam Rama with JP Morgan.

Anupam Rama^ Guys, congrats on the data and thanks for taking the question. Maybe a quick one from me. Ron, if you could give us some updated thoughts on the BEACON regulatory strategy and timelines and where you are in terms of enrollment in the Phase 3? Thanks so much.

Ron Squarer^ Hi, Anupam. Thanks for the question. So in terms of a regulatory path, as we've discussed, we are very carefully looking at the prospect of conducting an interim analysis on a subset of the patient population that will be recruited into the full Phase 3 trial, which has an overall survival endpoint. So we would be looking potentially at surrogates like a durable response or PFS and potentially seeking accelerated approval.

As soon as we've completed discussions with regulators, we'll be in a position to describe that.

And so in a way, that's perhaps the first event that might occur. And all we can really say about recruiting or recruitment is that it has been very strong and it's been strong really on the basis of the first response rate data, then the PFS and now showing even though overall survival hasn't yet been reached, the fact that the results are mature through -- in almost 13 months and have room of course to improve over that, I think that will help as well.

Operator^ And the next question will come from the line of Stephen Willey with Stifel.

Stephen Willey^ Yes, thanks for taking the questions. So, Ron, maybe just to kind of follow-up on the last question. If you do choose I guess to take an accelerated look at BEACON via a response rate, is there a minimum duration of follow-up that you would like to see in all patients before you decided to pull the trigger on unwinding? And then just secondly, I guess we saw the IMblaze data of Roche yesterday. You obviously have the 2 collaborations with Merck and Bristol and I believe you're driving the decision-making process with respect to the latter. So just kind of wondering how we should be thinking about the fate of any additional development here.

Ron Squarer^ Okay. So a couple questions there and I'd also be happy for Dr. Grothey to weigh in on IMblaze. And then I'll ask Dr. Sandor to comment on what may be relevant for regulatory approval. But as you've pointed out, IMblaze do not have a positive result. It was interesting that it appears that the addition of a MEK to PD-1 is better than a PD-1 alone. And I'll just give you our opinion and then we'll hear from Dr Grothey.

Our opinion is that in addition -- we have several differences in the approach we're using with Merck and BMS. First, we're really studying earlier line patients. So in the case of Merck, it's first and second line, in the case of BMS second and third. Next, we are using PD-1s in these studies, not PD-L1s. To the extent that that matters, we may find out. Next is we're adding a third agent or regimen. So in the case of Merck in order to recruit first and second line patients, we're using FOLFOX or FOLFIRI respectively. And in the case of BMS, we're adding ipilimumab. So you see many differences there. One last difference in the BMS collaboration, we're actually selecting for RAS patients. We don't know yet if that's going to help or not. We can always expand in the future if we feel it doesn't matter. But certainly the biology and the early thinking would suggest that RAS may have a better chance. So before we go to a potential accelerated path, perhaps Dr. Grothey could weigh in on the prospects for a MEK PD-1 plus another agent or regimen plan.

Axel Grothey^ Yes, happy to. So the IMblaze data were clearly a disappointment. On the other hand, I also saw exactly what you saw, that the addition of a MEK inhibitor to atezolizumab have actually lifted the combination on the level of regorafenib. We should not underestimate regorafenib as an active agent and we've seen actually a shift in terms

of better outcomes now with regorafenib in recent studies now that we know how to manage side effects and toxicities of regorafenib better. Unfortunately, we didn't beat regorafenib, but it still shows that it's an active agent when you talk about overall survival in the comparison here.

I really do believe that the addition of chemotherapy in earlier lines of therapy could be a game changer. We see the combination of chemotherapy plus an augmented immune oncology approach works very well in lung cancer. So I do believe this could be very different in an earlier line setting, in a different combination of setting and IMblaze might be kind of one of the sidestep of negative data that we still struggle with. And as a clinician, of course, I would have liked this to be different, but we need to learn about it and I don't think it's really closes the door for all these combinations that are ongoing right now.

Ron Squarer^ And with that, Victor, if you could address the question of the regulatory path. And then we're going to have to wrap up.

Victor Sandor^ So I think the question you're asking is specifically if we were to use an overall response rate type of endpoint as the regulatory endpoint what kind of follow-up we would need. I mean, I don't think that there's a straightforward answer to that in terms of if it's going to be 6 months or a year. I mean, I would say that even if we took a number like 6 months, for example, because of the recruitment period for the study, the majority of the patients obviously would have more than 6 months of follow-up. So you would have a range from more than a year through 6 months. So it's not that straightforward.

But I think that historically if you look at, for example, some of the immunotherapy approvals based on single-arm studies, 6 months is a bit of a benchmark in terms of looking at what's the durability of a response or what proportion of patients have a durable response beyond 6 months.

Ron Squarer^ Well, very good. As I mentioned, we had a limited window today. I want to thank Dr. Grothey and his fellow investigators for their assistance with this and other studies, as well as the patients who are participating and the employees at Array who support the work that we do.

We do have a PDUFA date coming up in the next, let's just say, few days. We have no reason to be concerned about or we're not aware of any issues related to our file at this point. So we look forward to receiving news in the not too distant future and making these 2 agents available first for BRAF melanoma.

And with that, I will close the call. Thank you all very much.

Operator^ Ladies and gentlemen, thank you for participating in today's conference. This does conclude your program. You may all disconnect. Everyone, have a great day.