Very good morning everyone. I'll be presenting the results of Delphi 301 which is a phase 2 study.
It's extended follow-up data on clinical benefit and safety.
We know that small cell lung cancer is a very aggressive cancer with very poor long-term prognosis. There are hardly any treatments which give a good PFS beyond the second line and once the patient has crossed the second line treatment, the overall survival is limited to just a few months.
Basically, DLL3, this is a delta like ligand 3. This is present within the cytoplasm of normal cells, but in small cell lung cancer, it is apparently expressed on the surface.
So, tarlatumab is a bi-specific T cell engager, bite immunotherapy, which targets this DLL3 on the small cell lung cancer cells and CD3 on the T cells and it causes the formation of a cytolitic synapse between these two cells and that causes T cell mediated cancer cell lysis.
So, at the primary analysis, Delphi 301 showed durable responses and a manageable safety profile that led to its FDA approval, accelerated approval in May 2024.
So, here we have the long-term outcomes. This was the basic trial design.
It was conducted in three parts. It included small cell lung cancer patients who had received at least two lines of therapy in the past with a measurable disease.
Part 1 was a dose evaluation phase where they tried to find out which dose had the best risk benefit ratio, 10 mg versus 100 mg.
And after about 30 patients were enrolled onto both these dosing regimens, then in Part 2, whichever gave the best risk benefit ratio, that dose was selected.
So, here the 10 mg dose was selected and taken forward. The primary endpoint of this trial was mainly the overall response rate as assessed by a blinded independent committee by Racist 1.1. And there were several other secondary endpoints like duration of response, progression-free survival and overall survival treatment, emergent adverse events, as well as some pharmacokinetic parameters and patient reported outcomes.
An important thing to note in the baseline characteristics is that almost one-third of the patients on both the dosing arms, 10 mg as well as 100 mg, received three or more lines of prior therapy. So, this was a very heavily pre-treated population.
And also, they included patients who had a PFS of less than 90 days on previous platinum therapy. DLL3 is expressed in almost 85 to 95 percent of the small cell lung cancer cells.
And that is what is seen even in this trial where 95 percent and above patients had the expression of DLL3.
And if you look at the objective response rate, which was the primary endpoint of this phase 2 trial, it was 40 percent with a disease control rate of 70 percent and three percent complete responses were seen. So, tarlata mapped 10 mg dose. 10 mg was the dose which was chosen ultimately because it had lesser side effects, lesser toxicity.
In a heavily pre-treated small cell lung cancer subset of patients, it gave an overall response rate of 40 percent, which is very remarkable.
The duration of response was around 9.7 months. The median time to response was 1.4 months.
And at the time of data cut off, these arrowheads are the patients who were continuing to respond where they had a sustained response even at the time of data cut off that was seen in about 43 percent of the patients.
Tumor shrinkage was seen in about 72 percent of the patients and around 7 months was the median duration of disease control.
26 percent of the patients even beyond one year, beyond 52 weeks, they had a sustained disease control, which is again a very remarkable thing.

The progression-free survival at the one-year time point, it was seen that nearly one-fourth of the patients was still progression-free on the 10 mg dosing arm, the median PFS being about 4.3 months.
Overall survival at the one-year time point was 57 percent and at the one-and-a-half year time point was 46 percent.
So the median OS was 15.2 months, which is again in a heavily pre-treated population of disease-like small cell lung cancer, which is a very remarkable number, more than a year median OS.
And irrespective of the progression-free interval after first-line platinum, whether it was less than 90 days or more than 90 days, the overall survival was similar even in patients who had a less than 90 day progression-free interval after first-line platinum.
The most common tarlata map related adverse events were mainly cytokine release syndrome.
So here, if you see in the dosing schedule, there is a 1 mg step dose, which is given.
1 mg is given on day 1. Tarlata map is a 60-minute infusion and that is followed by 10 mg on day 8, day 15 and then followed by a twice a week regimen that has continued.
Similarly, for 100 mg also, 1 mg was a step dose.
So one of the most common adverse events that was seen is cytokine release syndrome, as expected out of any other T cell mediated therapy.
It was a cytokine release syndrome that was seen in almost 53 percent, but the tolerability was very good.
It led to dose interruption in 16 percent of the patients, but complete drug discontinuation rates were very low. It was less than 5 percent.
And this step dose of 1 mg, which is given initially on day 1, is mainly one of the strategies that was adopted in order to reduce the incidence and severity of cytokine release syndrome and there were other insignificant adverse events as well.
Now, if you look at the immune effector cell mediated neurological syndrome, that is, IKANS, this was also mainly grade 1, grade 2 events.
It occurred within the first six months of initiating the treatment and all the events were grade 1, grade 2. In fact, there was no grade 3 toxicity that was seen with the 10 mg dosing.
CRS also mainly occurred with the first and second dose. The incidence was significantly lesser thereafter and most of the CRS events were also grade 1, grade 2.
So, to conclude, Delphi 301 with extended follow-up, the 10 mg 2 weekly regimen of tarlata map demonstrated a good durable responses, improved survival outcomes and long-term tolerability was also very good with no new safety signals and manageable side effect profile.
Now, the other part of my talk is what happened to the patients who had brain metastasis with and without brain metastasis when we analyze the data.
About 40 to 70 percent of small cell lung cancer patients have brain met set baseline and in Delphi 301, they included patients who had treated and stable brain metastasis. That's about 29 percent of the patients had brain metastasis in this study and more than 90 percent of them received radiation for the brain metastasis.
And if you analyze the 10 mg data set, if you see those who had brain metastasis and who did not have brain metastasis, the overall response rates were 55 percent in patients with brain met and about 52 percent in those who did not have brain met.
The PFS was around 7 months and the median OIS was 14 months. If you see the 10 mg and 100 mg together, the overall response rates were 45 percent median PFS of 5.6 months and median OIS was not reached.
So, whether patients had or did not have brain metastasis, it did not really impact. The ICANN's grade, it was the proportion of patients who developed ICANN's. It was a little higher in patients with brain metastasis, but this difference was not very significant.

So, it showed promising efficacy and a favorable risk benefit profile in patients who were previously treated small cell lung cancer patients who had stable brain metastasis.
In presence or absence of brain metastasis did not really affect the efficacy or the side effect profile of the drug. Thank you.