

1610

## Randomized preoperative window of opportunity (WOO) study with the CDK4/6 inhibitor abemaciclib in early breast cancer (EBC) patients and differential gene expression pathway analyses with palbociclib

M. Arnedos<sup>1</sup>, D. Chaltiel<sup>2</sup>, B. Cheaib<sup>1</sup>, D. Drubay<sup>2</sup>, D. Gentien<sup>3</sup>, A. Vieillefon<sup>3</sup>, V. Scott<sup>4</sup>, I. Bouakka<sup>5</sup>, J. Adam<sup>6</sup>, I.J. Garberis<sup>4</sup>, F. Rimareix<sup>7</sup>, N. Leymarie<sup>7</sup>, A.A. Viansone<sup>8</sup>, M. Lacroix-Triki<sup>9</sup>, S. Michiels<sup>2</sup>, F. André<sup>10</sup>

<sup>1</sup> Medical Oncology, Institut Gustave Roussy, Villejuif, France, <sup>2</sup> Team Oncostat, CESP, Institut Gustave Roussy, Villejuif, France, <sup>3</sup> Genomic Platform. Translational Research, Institut Curie, Paris, France, <sup>4</sup> Inserm Unit 981, Institut Gustave Roussy, Villejuif, France, <sup>5</sup> Research Department, Institut Gustave Roussy, Villejuif, France, <sup>6</sup> Pathology, Institut Gustave Roussy, Villejuif, France, <sup>7</sup> Surgical Department, Institut Gustave Roussy, Villejuif, France, <sup>8</sup> Department of Cancer Medicine, Institut Gustave Roussy, Villejuif, France, <sup>9</sup> Biology and Pathology Department, Institut Gustave Roussy, Villejuif, France <sup>10</sup> Breast Cancer Unit, Medical Oncology Department, Gustave Roussy - Cancer Campus, Villejuif, France

### Background

In our previous WOO study short-term palbociclib caused a profound inhibition in proliferation. Due to the different pattern of CDK target inhibition, we conducted a similar WOO trial with abemaciclib to determine its antiproliferative effect and to assess differences in GE array pathway analyses with palbociclib.

### Methods

Untreated EBC patients (n=105) were randomized 3:1 to abemaciclib 150mg twice daily for 14 days vs. no treatment. FFPE and frozen samples were taken at baseline and at surgery. Primary objective was antiproliferative response defined as natural logarithm of Ki67 expression at day 15 < 1. Immunostainings (Ki67, RB, pRB, p16, Cyclin D1, Cyclin E1, Cyclin E2, TILs, CD8+/FOXP3 ratio) and gene expression (GE) arrays were performed pre- and post-treatment. Pooled GE pathway analysis with GE arrays from our WOO trial with palbociclib and comparisons between drugs were performed.

### Results

In the ABC-POP trial, abemaciclib led to significant differences as compared to control in antiproliferative effect (71 vs. 8%; p < 0.001) and changes in Ki67 (p < 0.0001), pRB (p < 0.0001), Cyclin D1 (p = 0.047) and Cyclin E2 (p < 0.0001) by IHC. No significant predictive biomarkers were identified. Abemaciclib had significant effect on change from baseline in 63 genes mostly associated with cell cycle and proliferation. No genes were significantly associated with abemaciclib antiproliferative effect. In the pooled (N=168) GE pathway analysis with patients from ABC-POP and from the trial with palbociclib, CDK4/6 inhibition was associated to significant effect on E2F, G2M and mitotic spindle pathways. No differential effect on GE pathways was observed between abemaciclib and palbociclib.

### Conclusions

Short-term pre-operative abemaciclib was associated to significant antiproliferative effect as well as a change in cell cycle biomarkers like pRb, Cyclin D1 and Cyclin E2 by IHC and by GE array. Pooled GE pathway analyses with palbociclib treated patients showed significant effect on cell cycle pathways although no significant differences were seen between the two CDK4/6 inhibitors. Further analyses with the pooled GE arrays will be presented.

### Clinical trial identification

NCT02831530.

### Legal entity responsible for the study

Gustave Roussy Cancer Campus.

### Funding

Eli Lilly.

### Disclosure

M. Arnedos: Honoraria (self), Travel/Accommodation/Expenses: Novartis; Honoraria (self), Travel/Accommodation/Expenses: AstraZeneca; Advisory/Consultancy: Seattle Genetics; Honoraria (self), Research grant/Funding (institution): Pfizer; Research grant/Funding (institution): Eli Lilly. J. Adam: Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: BMS;

Advisory/Consultancy: Roche; Advisory/Consultancy: MSD; Advisory/Consultancy: Bayer. S. Michiels: Advisory/Consultancy: IDDI; Advisory/Consultancy: Janssen Cilag. F. André: Honoraria (institution), Advisory/Consultancy, Research grant/Funding (institution): Novartis; Honoraria (institution): Eli Lilly; Honoraria (institution), Research grant/Funding (institution): Pfizer; Honoraria (institution), Advisory/Consultancy, Research grant/Funding (institution): Daiichi; Honoraria (institution): Roche. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology