**CONFLICTS OF INTEREST**

This author has no conflicts of interest. Study is sponsored by Debiopharm.

**REFERENCES**

1. O’Dowd et al., Antitumor activity of the novel oral highly selective Wee1 inhibitor Debio 0123. AACR 2019 #4423.

**MAIN INCLUSION CRITERIA**

1. Age ≥ 18 years.
2. Adequate bone marrow function.
3. Life expectancy of at least 3 months in the best judgement of the Investigator.
4. Histology or cytology demonstrating a malignant solid tumor that has recurred or progressed following standard therapy and for which no standard therapy of proven benefit is available.
5. Sample tumor and/ or blood specimen available for TP53 mutation status.
6. Adequate organ function: Bilirubin ≤ 1.5 x upper limit of normal (ULN) or ≤ 3 x ULN in patients with brain tumors or a G1-3 brain metastasis. ALT and AST ≤ 2.5 x ULN. Creatinine clearance ≥ 50 ml/min or creatinine ≤ 1.5 x ULN and ≤ 2 x ULN in patients with brain tumors or a G1-3 brain metastasis. Platelets ≥ 75,000/μL and normal absolute neutrophil count. On Cycle 1 Day 3 (C1D3), LVEF ≥ 55% by MUGA scan or > 55% by echocardiogram (ECG), and no history of cardiotoxicity experienced after previous chemotherapy.
7. Adequate bone marrow function: Adequate bone marrow function.
8. Previous platinum-based chemotherapy (carboplatin or cisplatin).
9. Signed written informed consent before undertaking any study-related procedures.

**MAIN EXCLUSION CRITERIA**

1. History of other malignancies requiring active treatment in the last 6 months.
2. Non-squamous cell malignancies unless they are asymptomatic, stable on recent imaging (not > 3 months), and have not required active treatment in the last 3 months.
3. Patients with first or second-degree relatives who have been diagnosed with breast cancer or brain tumors and/or brain metastases unless they are asymptomatic, stable on recent imaging (not > 3 months), and have not required active treatment in the last 3 months.
4. Hematologic abnormalities: Hemoglobin ≤ 9 g/dL; platelets ≤ 75,000/μL; absolute neutrophil count ≤ 1,500/μL.
5. Hypersensitivity to carboplatin or any of the excipients.
6. Previous or concurrent treatment with another investigational anticancer product.
7. Overt dehiscence of a cardiac valve, history of congenital long QT syndrome, the presence in the screening ECG of a QRS duration > 130 msec, or a history of significant bradycardia.
8. History of second malignancy.
9. Left ventricular systolic dysfunction (ejection fraction < 55%)
10. History of second malignancy.
11. Hypersensitivity to carboplatin or any of the excipients.
12. Use of concomitant medications known to prolong QTc interval or with a known risk of QT prolongation.
13. Use of medications known to prolong QTc interval or with a known risk of QT prolongation.
14. Onset or increase in a risk factor for QT prolongation.
15. Absolute neutrophil count ≤ 1,500/μL.

**CLINICAL TRIAL INFORMATION**

NCT03968663
https://clinicaltrials.gov/ct2/show/NCT03968663

**CONCLUSIONS**

Debio 0123 is a highly selective and potent Wee1 inhibitor able to induce CDCC2/CDCC3 phosphorylation currently being investigated in First in line in combination with carboplatin in patients with advanced solid tumors.

**DOSE LEVEL AND TREATMENT DURATION**

1. Dose level 1 and 2 well tolerated with manageable toxicity.

**ACKNOWLEDGMENTS**

This manuscript has been supported by Debiopharm International S.A., Lausanne, Switzerland.

**ABSTRACT #3893**

**FIRST-IN-HUMAN PHASE 1 STUDY OF A NOVEL ORAL WEE1 INHIBITOR (DEBIO 0123) IN COMBINATION WITH CARBOPLATIN IN PATIENTS WITH ADVANCED SOLID TUMORS**

**THERAPY**

The Wee1 tyrosine kinase is activated upon DNA damage and regulates the G2-M cell cycle checkpoint. Inhibition of Wee1, in conjunction with additional genetic alterations and/or addition of a DNA-damaging agent, results in mitotic catastrophe and apoptosis of cancer cells, being an attractive approach for treating cancer. Debio 0123 is a potent and highly specific Wee1 inhibitor with an IC50 in the low nanomolar range. Debio 0123 combination with carboplatin was synergic in vitro. In vivo, Debio 0123 was demonstrated to increase anti-tumor activity in combination with carboplatin in models where neither agent was active alone.

**PUBLIC HEALTH IMPACT**

Debio 0123 is a novel Wee1 inhibitor with demonstrated activity in combination with carboplatin.

**METHODS**

This is a phase 1, multi-center, open-label, dose escalation study of Debio 0123 as monotherapy (first cycle only) and in combination with carboplatin, from cycle 2 in subjects with advanced solid tumors that recurred or progressed following prior platinum therapy. The Wee1 tyrosine kinase is activated upon DNA damage and regulates the G2-M cell cycle checkpoint. Inhibition of Wee1, in conjunction with additional genetic alterations and/or addition of a DNA-damaging agent, results in mitotic catastrophe and apoptosis of cancer cells, being an attractive approach for treating cancer. Debio 0123 is a potent and highly specific Wee1 inhibitor with an IC50 in the low nanomolar range. Debio 0123 combination with carboplatin was synergic in vitro. In vivo, Debio 0123 was demonstrated to increase anti-tumor activity in combination with carboplatin in models where neither agent was active alone.

**CONFLICTS OF INTEREST**

This author has no conflicts of interest. Study is sponsored by Debiopharm.

**REFERENCES**

1. O’Dowd et al., Antitumor activity of the novel oral highly selective Wee1 inhibitor Debio 0123. AACR 2019 #4423.