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Ribociclib plus letrozole and concomitant palliative radiotherapy for metastatic breast cancer

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Keywords: breast cancer; concomitant radiotherapy; ribociclib; safety.

32 **Abstract**

33 Ribociclib is a CDK4-6 inhibitor recently approved by the Food and Drug Administration (FDA) and the European
34 Medicines Agency (EMA) as first-line treatment for metastatic breast cancer (MBC). The pivotal trial showed a
35 significant improvement in progression-free survival when compared to endocrine therapy alone. However, having a
36 challenging toxicity profile in comparison with exclusive endocrine therapy, safety may be a concern when combined to
37 radiotherapy (RT) with palliative approach.

38 There are no available published data regarding the combination of ribociclib and palliative RT. We reported our
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40 (Florence, Italy) giving palliative RT concomitant to ribociclib plus letrozole as first-line treatment for MBC.

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63 **Viewpoints and Debates**

64 Ribociclib (Kisqali®; Novartis, Basel, Switzerland) is a CDK4-6 inhibitor recently approved by the Food and Drug
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69 concern when combined to radiotherapy (RT) with palliative approach. Nevertheless, inhibition of CDK4/6 has shown
70 to exert a protective effect on radiation-induced gastrointestinal toxicity in a preclinical model [2]. Therefore, the
71 association of this class of drugs with RT could represent a beneficial combination.

72 There are no available published data regarding the combination of ribociclib and palliative RT in a clinical setting. A
73 recently published preliminary report on five patients treated with palbociclib and radiation at the Institut Curie (Paris,
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75 We reported our preliminary experience on the first five patients treated at the Radiation Oncology Unit of the Florence
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79 Main patients' series characteristics are summarized in *Table 1*. In all cases, RT was prescribed with palliative/analgesic
80 intent due to symptomatic bone metastases. Two patients had bone-only disease, three patients both bone and visceral
81 disease (two lung, one liver).

82 Hematological and non-hematological **toxicities were assessed during the second 21-days cycle of ribociclib, following**
83 **the concomitant delivery of RT and the first cycle of ribociclib**. Major recorded adverse events confirmed a safety
84 profile of the combined approach in line with main published data [1,4,5]. No RT course was suspended, and all
85 patients had pain relief.

86 Ribociclib treatment suspension was required in two cases, for two weeks. Treatment recovery (first dose reduction;
87 400 mg; 2 x 200-mg tablets) was observed in both cases, while letrozole was never suspended.

88 At time of the present analysis, all the patients are still on first-line treatment: three patients received four cycles and
89 two patients five cycles of ribociclib. At 3-month assessment (clinical visit, thorax/abdomen computed tomography
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91 Even though the toxicity profile of concomitant ribociclib and RT requires further large investigations, our very
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Conflicts of interest statement

None declared.

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Table 1

Table 1. Main patients and treatments characteristics.

| Case | Age | PS | RT treated site | Dose (Gy)/Fx | Technique | Ribociclib cycle | G3-4 hematological toxicity* | G3-4 non hematological toxicity* | RT suspension required | Pain relief ^o | Ribociclib suspension required* | Weeks of suspension |
|------|-----|----|---------------------------------|-----------------|-----------|---------------------|------------------------------------|--|------------------------------|-----------------------------|---------------------------------------|------------------------|
| 1 | 71 | 0 | Left femoral neck | 30/5 | VMAT | 1 | Neutropenia | No | No | Yes | Yes | 2 |
| 2 | 55 | 0 | Bilateral femoral neck | 20/5 | 3DCRT | 1 | No | No | No | Yes | No | 0 |
| 3 | 76 | 2 | Right hip | 20/5 | 3DCRT | 1 | No | Diarrhea Vomiting | No | Yes | Yes | 2 |
| 4 | 79 | 1 | Lumbar spine (L2-L3) | 20/5 | 3DCRT | 1 | No | No | No | Yes | No | 0 |
| 5 | 36 | 0 | Cervical/thoracic spine (C3-T2) | 20/5 | 3DCRT | 1 | No | No | No | Yes | No | 0 |

Abbreviations: PS, performance status; Dose/fx, total dose (Gy)/number of fractions; G3-4, grade 3-4; RT, radiotherapy; VMAT, volumetric modulated arc therapy; 3DCRT, 3-dimensional conformal radiotherapy.

*Toxicity recorded after the cycle of combined treatment ribociclib/letrozole with palliative radiation.

^oIf pain at palliative radiation start.

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