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1 **Ribociclib plus letrozole and concomitant palliative radiotherapy for metastatic breast cancer**

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

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32 **Abstract**

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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.

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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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70 to exert a protective effect on radiation-induced gastrointestinal toxicity in a preclinical model [2]. Therefore, the
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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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77 consecutive days of treatment, followed by 7 days off treatment) plus letrozole (2.5 mg tablet; once daily throughout the
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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**
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86 Ribociclib treatment suspension was required in two cases, for two weeks. Treatment recovery (first dose reduction;
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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.

Highlights

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