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[1*]Icro Meattini, [1]Isacco Desideri, [1]Vieri Scotti, [1]Gabriele Simontacchi, and [1]Lorenzo Livi

[1]*Radiation Oncology Unit, Oncology Department, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Florence, Italy*

*Corresponding Author:

Icro Meattini, MD

Radiation Oncology Unit, Oncology Department

Azienda Ospedaliero-Universitaria Careggi, University of Florence

Largo G. A. Brambilla 3, 50134, Florence, Italy

Tel: +39-055-7947719; fax +39-055-4379930

e-mail: icro.meattini@unifi.it

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

Abstract

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

There are no available published data regarding the combination of ribociclib and palliative RT. We reported our preliminary experience on the first five patients treated at the Radiation Oncology Unit of the Florence University (Florence, Italy) giving palliative RT concomitant to ribociclib plus letrozole as first-line treatment for MBC.

Viewpoints and Debates

Ribociclib (Kisqali®; Novartis, Basel, Switzerland) is a CDK4-6 inhibitor recently approved by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) as first-line treatment for metastatic breast cancer (MBC). The pivotal trial showed a significant improvement in progression-free survival when compared to endocrine therapy alone [1].

However, having a challenging toxicity profile in comparison with exclusive endocrine therapy, safety may be a concern when combined to radiotherapy (RT) with palliative approach. Nevertheless, inhibition of CDK4/6 has shown to exert a protective effect on radiation-induced gastrointestinal toxicity in a preclinical model [2]. Therefore, the association of this class of drugs with RT could represent a beneficial combination.

There are no available published data regarding the combination of ribociclib and palliative RT in a clinical setting. A recently published preliminary report on five patients treated with palbociclib and radiation at the Institut Curie (Paris, France) showed encouraging results [3].

We reported our preliminary experience on the first five patients treated at the Radiation Oncology Unit of the Florence University (Florence, Italy) giving palliative RT concomitant to ribociclib (600 mg once daily; 3 × 200-mg tablets; 21 consecutive days of treatment, followed by 7 days off treatment) plus letrozole (2.5 mg tablet; once daily throughout the 28-day cycle) as first-line treatment for MBC.

Main patients' series characteristics are summarized in *Table 1*. In all cases, RT was prescribed with palliative/analgesic intent due to symptomatic bone metastases. Two patients had bone-only disease, three patients both bone and visceral disease (two lung, one liver).

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

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

At time of the present analysis, all the patients are still on first-line treatment: three patients received four cycles and two patients five cycles of ribociclib. At 3-month assessment (clinical visit, thorax/abdomen computed tomography scan, bone scan), three stable disease and two partial response were observed.

Even though the toxicity profile of concomitant ribociclib and RT requires further large investigations, our very preliminary data showed encouraging results and a safety in line with data deriving from pivotal trials. Prospective cooperative data collection initiative on combined strategy is warranted.

Conflicts of interest statement

None declared.

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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°	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.

°If pain at palliative radiation start.

Highlights

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