



## Elective pelvic nodal irradiation for elderly patients with high-risk prostate cancer: A more patient-oriented approach

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### ABSTRACT

The role of elective pelvic nodal irradiation (EPNI) for high-risk prostate cancer (hrPC) management is still an open issue, especially for the elderly patients. It is unclear whether older patients can experience the same benefit from the treatment strategies used for younger men. Hence, in absence of solid data, it appears reasonable to pursue a shared decision-making process so that older patients can express their informed preferences about the different treatment options. In this letter, we discuss why caution appears reasonable on EPNI trade-off in hrPC patients aged 75 years or more.

### Dear Editor,

The role of elective pelvic nodal irradiation (EPNI) for prostate cancer (PC) management is still an open issue, especially for the elderly patients. Due to population aging, recent epidemiological data shows how PC incidence peak has moved towards 70–75 years of age over time, with a stable mortality across all European countries [1]. Progressively, we will observe a rise in the number of older men with PC. This population is underrepresented in clinical studies (<40 %) and generally suffers from more comorbidities [2]. Consequently, it is unclear whether older patients can experience the same benefit from the treatment strategies used for younger men, EPNI included.

Thus, we read with great interest the recent article of Glicksman and colleagues [3]. The authors examined three studies, namely the pHART2, the SATURN, and the 5STAR, investigating the pros and cons of EPNI delivered with different irradiation schedules [3]. In these works, median population age ranged between 74 and 77 years, with most of the patients affected by high-risk PC (hrPC). The authors reported no difference in terms of 3-year recurrences free survival and late toxicity. However, they highlighted a worse acute grade  $\geq 2$  genitourinary (GU) toxicity associated with the ultra-hypofractionation regime. To our view, this paper helps keeping the discussion alive on EPNI delicate risk–benefit balance for older hrPC patients. We share Glicksman and colleagues' enthusiasm for the forthcoming trials investigating different irradiation schedules for EPNI delivery. Nonetheless, with reference to the older patients, we warn not to overlook EPNI potential toxicities. Considering available Literature, the POP-RT trial is currently the most explicative study to discuss this topic [4]. The trial specifically investigated the role of EPNI delivered with modern radiotherapy approach, in a population affected by hrPC. At five years, the authors reported a 60 % and 77 % improvement in disease free survival (DFS) and biochemical failure-free survival (BFFS), respectively, by adding EPNI to prostate irradiation and androgen deprivation therapy (DFS: HR, 0.40; 95 %CI, 0.22 to 0.73; p-value < 0.05 – BFFS: HR, 0.23 95 %CI, 0.10 to 0.52; p-value < 0.05) [4]. Based on these positive data, they suggested that EPNI should be routinely considered

as standard for hrPC patients, although no difference in overall survival (OS) was observed. Moreover, it is noteworthy how EPNI benefit was debatable for patients >66 years (BFFS: HR, 0.66, 95 %CI 0.21 to 2.10). Consequently, caution appears reasonable evaluating the EPNI 5-year trade-off in older hrPC patients (Fig. 1).

At five years, the number needed to treat (NNT) to avoid a recurrence and a distant metastasis onset amounted to 5 and 8 patients, respectively. However, 9 patients were required to receive EPNI to develop one G2-G3 GU late toxicity.

It is possible to argue that data are still immature to draw a definitive conclusion because a longer follow up is necessary. However, this argument can concurrently be used both to support and not support EPNI recommendation in this population. Moreover, it is still unclear to what extent the interplay between EPNI and the new androgen receptor signalling pathway inhibitors (ARSI) can impact on cancer specific survival for older patients. Treatment intensification for hrPC might not represent the most appropriate strategy for all cases. Considering the new available therapeutic strategies, we should ponder that older patients may benefit from a less aggressive approach, as a recurrence does not always mean a reduced survival but could imply a reduced burden of treatment related toxicity. According to the International Society of Geriatric Oncology (SIOG) the 75 year-of-age can be considered an appropriate threshold to define the category of the elderly [5]. As these oncological patients tend to be more keen to treatment-related toxicities, the trade-off between quantity and quality of life should strongly be accounted in the cancer management strategy.

In absence of resolute studies, we encourage a shared decision-making process when EPNI delivery is evaluated for hrPC patients  $\geq 75$  years of age, since their preferences should not be neglected. This means shifting from a disease-oriented to a more patient-oriented approach.

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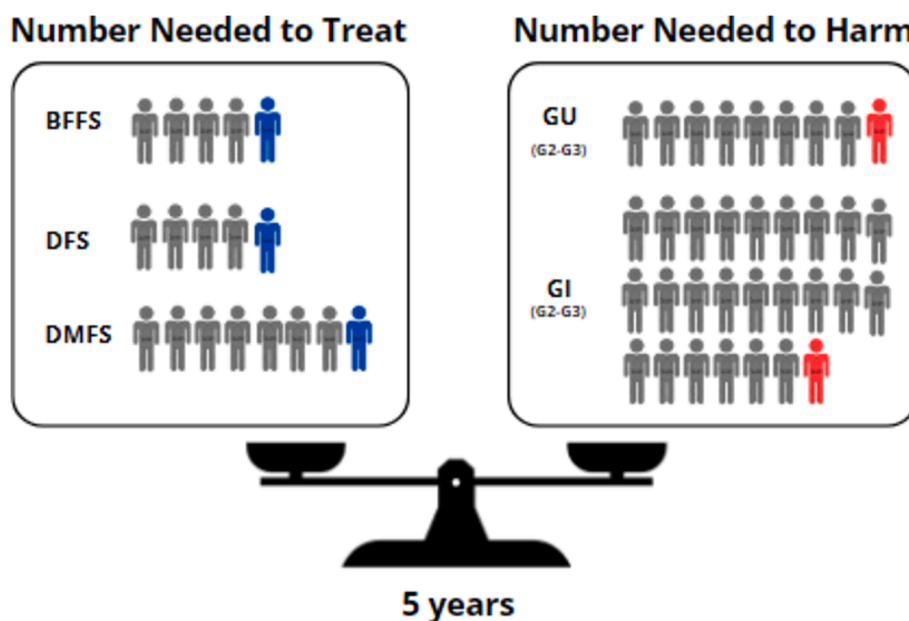
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**Fig. 1.** On one side, the image illustrates the number needed to treat at 5 years for biochemical failure free survival (BFFS), disease free survival (DFS), and distant metastasis free survival (DMFS). On the other side, again at 5 years, it is displayed the number needed to harm relating to G2-G3 genitourinary (GU) and gastrointestinal (GI) toxicity.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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