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LETTER TO THE EDITOR

From treatment escalation to ultra de-intensification: When androgen-deprivation therapy alone remains a rational choice in metastatic hormone-sensitive prostate cancer

We read with great interest the article by Tsung et al. on the evolving management of metastatic hormone-sensitive prostate cancer (mHSPC) and the ongoing debate between treatment intensification and de-intensification.[1] We would like to expand this discussion by pointing out a relevant clinical scenario that is often overlooked: the potential role of *androgen-deprivation therapy (ADT) alone—without the addition of chemotherapy or novel hormonal agents*—in carefully selected patients.

Although robust evidence supports early intensification with ADT plus a novel hormonal agent or chemotherapy,[2] there remains a subset of patients for whom ADT monotherapy may be a proportionate and patient-centered option. This is particularly the case for men with metachronous and low-volume disease, as defined by conventional imaging, for men of advanced age or those with frailty, in whom competing risks may outweigh the incremental survival gains; for individuals with substantial comorbidities, such as cardiovascular disease, that confer heightened vulnerability to systemic toxicities; and for patients with poor performance status, in whom the tolerability of intensified regimens is limited (Table 1).

TABLE 1 Clinical features guiding consideration of androgen-deprivation monotherapy in metastatic hormone-resistant prostate cancer.

Disease burden	Low-volume disease[a]
Age and frailty	Advanced age, frailty, or limited life expectancy
Comorbidities	Significant cardiovascular, metabolic, or other systemic comorbidities increasing treatment risk
Performance status	ECOG ≥2 or Karnofsky <70, with reduced tolerance to systemic therapies
Other prognostic factors	Low BMI, sarcopenia, or competing risks of mortality within 2–3 years
Patient preferences	Desire to avoid treatment toxicity or complex therapeutic regimens

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.

[a]Low-volume was determined by conventional imaging (e.g., four or less bone lesions, no visceral metastases).

Real-world practice indicates that older and functionally impaired patients are less likely to receive intensification, and retrospective analyses suggest that individuals with limited life expectancy, low body mass index, or high comorbidity burden may die from competing causes before castration resistance develops—rendering escalation of questionable net benefit in some patients.[3,4] Moreover, although many patients with mHSPC progress to castration-resistant disease within 2–3 years, the *marginal utility* of intensification may be attenuated in these vulnerable subgroups, particularly when health-related quality of life is prioritized.[5]

Therefore, believe that prospective studies should explicitly investigate the role of ADT monotherapy in this context, incorporating validated geriatric assessments, comorbidity indices, and patient-reported outcomes. A truly personalized treatment paradigm for mHSPC not only should embrace therapeutic escalation where appropriate but also should acknowledge the continued relevance of judicious de-escalation to ADT alone in carefully defined clinical scenarios.

AUTHOR CONTRIBUTIONS

Giandomenico Roviello: Conceptualization; writing—original draft; data curation; supervision. **Martina Catalano**: Conceptualization; methodology; supervision; writing—review and editing. **Lorenzo Antonuzzo**: Conceptualization; supervision; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors disclosed no conflicts of interest.

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REFERENCES

1. Tsung I, Yentz SE, Reichert ZR. Controversies in metastatic hormone-sensitive prostate cancer. *Cancer*. 2025;131(16):e70030. doi:10.1002/cncr.70030
2. Wala J, Nguyen P, Pomerantz M. Early treatment intensification in metastatic hormone-sensitive prostate cancer. *J Clin Oncol*. 2023; 41(20):3584-3590. doi:10.1200/JCO.23.00723
3. Eule CJ, Kuna EM, Robin TP, Gershman B, Flaig TW, Kim SP. Treatment intensification in metastatic hormone-sensitive prostate cancer: an analysis of real-world practice patterns from the CancerLinQ database. *Urol Oncol*. 2024;42(12):447.e17-447.e24. doi:10.1016/j.urolonc.2024.07.002
4. Chong B, Saad M, Chong TW, et al. Selective treatment de-escalation in advanced prostate cancer: have we come full circle? *BJU Int*. 2025;135(5):733-740. doi:10.1111/bju.16632
5. Ávila C, González-Montero J, Rojas CI, Madan RA, Burotto M. Current landscape in first-line treatment of metastatic hormone sensitive prostate cancer: a cost-effectiveness focused review. *Oncologist*. 2025;30(5):oyaf095. doi:10.1093/oncolo/oyaf095