

## The Role of Active Surveillance in Patients with Low-Risk Prostate Adenocarcinoma Harboring a Germline Brca2 Mutation: A Critical Discussion of Recent Evidence

Y. Alaoui<sup>1\*</sup>, O. Bentaleb<sup>1</sup>, S. Lafdali<sup>1</sup>, A. Chatar<sup>1</sup>, M. A. Lakmichi<sup>1</sup>, Z. Dahami<sup>1</sup>, A. Mamad<sup>2</sup>, A. Bibat<sup>2</sup>, M.A. Elafari<sup>2</sup>, A. Slaoui<sup>2</sup>, K. Elkhader<sup>2</sup>, I. Sarf<sup>1</sup>

<sup>1</sup>Department of Urology, Errazi Hospital, Mohammed VI University Hospital Center of Marrakech

<sup>2</sup>Urology B Department, Ibn Sina Hospital, University Hospital Center Ibn Sina, Mohammed V University, Rabat, Morocco

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\*Corresponding author: Y. Alaoui

Department of Urology, Errazi Hospital, Mohammed VI University Hospital Center of Marrakech

### Abstract

### Case Report

Active surveillance (AS) has become the standard management strategy for low-risk localized prostate cancer in the general population because of its excellent long-term oncologic outcomes and its ability to reduce overtreatment [1,2]. However, its role in patients carrying a germline *BRCA2* mutation remains uncertain. Indeed, *BRCA2* is associated with an increased risk of prostate cancer, earlier onset, and more aggressive disease, with a higher risk of metastasis and poorer cancer-specific survival [1-3]. In this context, applying conventional AS criteria to this population raises a major question: does an apparently low-risk cancer in a *BRCA2* carrier truly represent indolent disease, or a disease that may be underestimated at diagnosis? The 2024–2026 French CCAFU recommendations and the 2026 EAU guidelines acknowledge the unfavorable prognostic impact of *BRCA2* while also emphasizing that no high-level evidence currently supports systematically excluding these patients from AS [1,2]. Available data mainly suggest an increased risk of reclassification in familial or hereditary settings, without definitive *BRCA2*-specific evidence [1,4]. As of 2026, AS may therefore be considered in highly selected patients, but only after rigorous initial characterization with multiparametric MRI and appropriate biopsy assessment, clear patient counseling, and intensified follow-up [1,2].

**Keywords:** prostate cancer; *BRCA2*; active surveillance; low risk; genetic predisposition; reclassification; prostate MRI.

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## INTRODUCTION

Active surveillance has become a central component of contemporary management for low-risk localized prostate cancer. Its aim is to delay, or even avoid, radical treatment in patients with tumors considered to have low biological potential, while preserving the option of curative therapy in the event of progression. The 2024–2026 French CCAFU recommendations confirm that AS is the reference treatment in this clinical setting, and European recommendations likewise state that it should be regarded as the standard of care for appropriately selected patients with sufficient life expectancy [1,2].

This approach becomes more challenging when a major inherited risk factor is identified. Among prostate cancer predisposition genes, **BRCA2** is particularly important because of its clear association

with a higher risk of clinically significant prostate cancer, younger age at onset, and worse oncologic outcomes. The 2024 *JAMA Oncology* review highlighted that pathogenic *BRCA1/2* variants, especially *BRCA2*, have major implications in men regarding cancer risk estimation, early detection strategies, and oncologic management [3]. The 2026 French and European guidelines are consistent with this view and recognize *BRCA2* as an adverse prognostic factor [1,2].

The issue is therefore no longer simply whether AS is effective in low-risk disease, but whether it remains appropriate in a patient whose biological background suggests a higher probability of aggressive behavior. In other words, can a prostate adenocarcinoma classified as “low risk” in a *BRCA2* carrier be expected to behave in the same way as a low-risk cancer arising in the general population? This tension between therapeutic

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standardization and inherited risk forms the basis of the present discussion [1-3].

## DISCUSSION

In the general population, the legitimacy of active surveillance for low-risk prostate cancer is no longer in question. Both French and European recommendations present it as the preferred option because it reduces overtreatment without compromising oncologic outcomes in properly evaluated patients [1,2]. Contemporary data also emphasize the contribution of multiparametric MRI to both initial selection and follow-up, which has improved the safety of this strategy compared with older biopsy-only cohorts [1,2].

In patients carrying a germline *BRCA2* mutation, the main difficulty is that the underlying tumor biology does not correspond to that of the general population. Updated French recommendations state that *BRCA2* mutations are associated with more aggressive forms of prostate cancer and reduced cancer-specific and overall survival [1]. The 2026 EAU guidelines likewise describe *BRCA2* as an independent determinant of poorer prognosis [2]. This means that even when disease appears clinically limited and histologically favorable, the clinician must keep in mind that the true risk may be higher than that suggested by conventional criteria alone [1-3].

This concern is first reflected in the possibility of *initial understaging or undergrading*. Active surveillance is safe only if the tumor has been accurately characterized at baseline. In *BRCA2* carriers, there is concern that insufficient sampling or incomplete imaging may fail to detect more extensive or higher-grade disease. This is precisely why French recommendations stress the importance of MRI, appropriate biopsy sampling, and early reassessment to exclude a sampling error [1]. This technical rigor, already essential in the general population, becomes even more critical in genetically predisposed patients [1,2].

A second reason for caution is the risk of *reclassification* or progression during AS. The 2024–2026 CCAFU recommendations indicate that a family history of prostate cancer or *BRCA*-spectrum cancers has been associated with a higher risk of reclassification [1]. The 2024 meta-analysis published in *Investigative and Clinical Urology* supports this signal: among patients managed with AS, a family history of prostate cancer was associated with an increased risk of progression, with a pooled adjusted hazard ratio of **1.31** (95% CI 1.16–1.48) [4].

However, methodological caution is essential. Data regarding family history or *BRCA*-spectrum cancers cannot be considered equivalent to data specifically addressing patients with a confirmed germline *BRCA2* mutation. This distinction is explicitly acknowledged in the French recommendations, which

recognize the signal of increased risk but also state that no high-level study has specifically evaluated AS outcomes in *BRCA*-mutated patients [1]. This lack of direct evidence prevents both excessive reassurance and dogmatic exclusion of all *BRCA2* carriers from AS [1,2].

From a practical standpoint, this leads to an intermediate position. A *BRCA2* mutation should probably not be considered an absolute contraindication to active surveillance, but neither can it be ignored in treatment decision-making. The French recommendations are explicit on this point: a mutated patient should not be excluded from AS solely on the basis of the mutation if the disease otherwise shows favorable characteristics [1]. This wording supports an individualized rather than binary approach [1,2].

The potential benefit of AS in a *BRCA2* carrier with low-risk prostate adenocarcinoma therefore remains theoretically real. As in the general population, AS may help avoid the adverse urinary, sexual, and functional consequences of radical prostatectomy or radiotherapy in a patient whose tumor is genuinely indolent. This potential benefit is particularly relevant in younger men, who are often highly concerned about quality-of-life preservation. However, such benefit is acceptable only at the cost of much stricter selection. It seems reasonable to reserve this strategy for patients with truly low-risk disease, high-quality MRI, concordant targeted and systematic biopsies, absence of adverse histologic features, and a clear understanding of the scientific uncertainty surrounding their individual situation [1,2].

In other words, in *BRCA2* carriers, the key issue is not so much whether active surveillance is theoretically possible, but rather under what *conditions it remains acceptable*. These conditions are necessarily more demanding than in the general population. They imply a lower threshold for reconsidering the initial indication, early reassessment, and probably less tolerance for discordance between biologic, radiologic, and histologic findings. Recent work on modern AS increasingly favors a personalized approach based on MRI and refined risk stratification; this logic is particularly applicable to *BRCA2* carriers [1,2].

It must also be emphasized that the current literature remains insufficient to establish dedicated AS algorithms for this population. Major guidelines recognize the importance of *BRCA2*, but do not yet propose a specific AS protocol because direct evidence is lacking [1,2]. Therefore, in 2026, decision-making still depends on individualized assessment, ideally within a multidisciplinary setting integrating MRI findings, histology, family history, genetic status, age, life expectancy, and patient preferences [1-3].

## CONCLUSION

As of 2026, active surveillance remains the standard of care for low-risk localized prostate cancer in the general population, but its role in patients carrying a germline *BRCA2* mutation must be approached with substantially greater caution [1,2]. Available evidence supports the idea that *BRCA2* is associated with more aggressive tumor biology and a higher likelihood of progression or reclassification in hereditary contexts, although there is still insufficient evidence to justify systematically excluding these patients from a conservative strategy [1-4].

The most defensible position is therefore the following: a *BRCA2* mutation is not an absolute contraindication to active surveillance in a patient with low-risk prostate adenocarcinoma, but it requires much stricter selection, optimal baseline characterization using MRI and appropriate biopsy assessment, transparent discussion of the current level of uncertainty, and more intensive follow-up than in the general population [1,2].

In practice, AS in these patients may be possible, but it should never be routine.

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