Félix Guerrero Ramos, Uro-Oncology Unit, Hospital Universitario 12 de Octubre. ROC Clinic. @DrFelixGuerrero

NEW ALTERNATIVES FOR THE MANAGEMENT OF NON-MUSCLE-INVASIVE BLADDER CANCER BCG UNRESPONSIVE

Given the **high rate of progression of bladder tumors to muscle-invasive disease,** any treatment other than radical cystectomy should be considered inferior in oncological terms (evidence level 3). **BCG (bacillus Calmette-Guérin) non-responsive CIS (carcinoma in situ) disease has a worse prognosis than papillary disease (high-grade Ta/T1).**

Currently, numerous molecules are being studied for this stage of the disease, some of them even approved by the FDA (Food and Drug Administration**), but none by the EMA (**European Medicines Agency**).**

In order to standardize the criteria for the approval of new treatments, the FDA established minimum response and duration rates. These objectives are applicable to the BCG non-responding CIS:

6-month complete response rate (CR):
50%
Response Duration (DR) in responders:
30% to 12 months
25% to 18 months

These are the **main treatments that have reported results in BCG-nonresponsive CIS disease:**

Drug	Route	CR Rate	DR 12m	DR 18m	FDA Approved	Toxicity grade 3 or higher
FDA Recommendation	***Any***	***50% 6 months***	***30%***	***25%***	***N/A***	***N/A***
Pembrolizumab	Intravenous	41% 3 months	46%	N/A	Yes	13%
Atezolizumab	Intravenous	42% 3 months	48.9%	N/A	No	16%
Nadofaragene firadenovec	Intravesical	53.4% 3 months	45.5%	N/A	Yes	4%
BCG + Nogapendekin alfa-inbakicept (N-803)	Intravesical	71% anytime	61.6%	N/A	No	23%
TAR-200	Intravesical (device)	72.7% at any time	N/A	N/A	No	N/A

Regarding **papillary disease without CIS that does not respond to BCG,** when the tumor is resected with transurethral resection, the result to be measured will be **high-grade recurrence-free survival (RFS),** establishing in this case the FDA a level of 30% and 25% in RFS at 12 and 18 months, respectively. There are no drug approvals for this group of patients.

Drug	Route	RFS 3m	RFS 12m	RFS 18m
FDA Recommendation	***Any***	***N/A***	***30%***	***25%***
Pembrolizumab	Intravenous	N/A	43.5%	34.9%
Nadofaragene firadenovec	Intravesical	72.9%	43.8%	N/A
BCG + Nogapendekin alfa-inbakicept (N-803)	Intravesical	N/A	55.4%	48.3%
TAR-210 (erdafitinib)	Intravesical (device)	82%	N/A	N/A

REFERENCES:
1. EAU Guidelines NMIBC 2023, 2. Huguet J, Actas Urol Esp 2023. 3. Guerrero-Ramos F, Actas Urol Esp 2023. 4. Balar AV, Lancet Oncol 2021. 5. Negro P, ASCO 2021. 6. Boorjian SA, Lancet Oncol 2021. 7. Chamie K, Evidencia NEJM 2022. 8. Daneshmand S, AUA 2023. 9. Vilaseca A, ESMO 2023. 10. Necchi A, ASCO-GU 2023