



## OncoFlash – Research Updates in a Flash! (May edition)

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### 1. Can Tocovid SupraBio and pentoxifylline improve the symptoms of late gastrointestinal (GI) toxicity following pelvic radiotherapy (RT)?

Randomised single centre double-blind placebo-controlled phase II trial of Tocovid SupraBio in combination with pentoxifylline in patients suffering long-term gastrointestinal adverse effects of radiotherapy for pelvic cancer: The PPALM study. Andreyev, H.J.N. et al. *Radiother and Oncol*, 2022 [1].

- Single centre, double-blind phase II trial of 62 patients who received radical pelvic RT for either T1-4N0-2M0 prostate (55%), gynaecological (34%), anal (10%) or rectal (1%) cancer.
- Minimum follow-up of at least 12 months post RT required and patients had to be experiencing GI symptoms attributable to RT of  $\geq$  grade 2 as per CTCAE v4 or grade 1 with difficult intermittent symptoms.
- Patients were randomised by symptom severity stratification in a 2:1 ratio to receive Tocovid SupraBio plus pentoxifylline twice daily for 12 months or placebo.
- There were no reported differences in mean change from baseline in bowel symptom severity scores, quality of life (QoL) scores or adverse events between the two groups.
- Bloods tests taken assessing inflammatory cytokines showed significantly reduced levels in the treatment group, suggesting a trend of reduced inflammation with treatment.
- The study closed prematurely and as such the authors report that it would be rash to conclude that their intervention has no useful role and further focused studies would be helpful.

### 2. Early-stage oropharyngeal squamous cell cancer (OPSCC) – can we choose between primary surgery and primary (chemo)RT?

Randomized Trial of Radiotherapy Versus Transoral Robotic Surgery for Oropharyngeal Squamous Cell Carcinoma: Long-Term Results of the ORATOR Trial. Nichols A. C. et al. *J Clin Oncol*, 2022 [2].

- Phase II trial recruited 68 patients with T1-T2, N0-2 (<4cm) OPSCC. 88% were p16 positive. They were randomly assigned to 70Gy in 35 fractions of radiotherapy (with concurrent platinum-based chemotherapy if node positive) or transoral robotic surgery with neck dissection.
- Primary outcome measure defined as swallowing related QoL at one year. Initial results showed primary RT provided statistically superior swallowing QoL but did not meet clinically significant pre-defined end points. This is echoed in now published 3-year follow-up data with a statistical difference noted but again no clinically meaningful difference between the two arms.
- Of note in the surgical arm, 29% received surgery alone but 47% had post-operative RT and 24% received post-operative chemo-RT.
- Post hoc subgroup analysis to be interpreted with caution given small sample size but suggested improvement for base of tongue cancers and node positive patients in primary (chemo)RT arm.

### 3. Can the use of nitroglycerin (NTG) alongside whole brain radiotherapy (WBRT) benefit non-small cell lung cancer (NSCLC) patients with brain metastases?

Nitroglycerin plus whole brain radiotherapy for brain metastases in non-small cell lung cancer patients: A randomized, open-label, phase II clinical trial. Arrieta, O et al. *Int J Radiat Oncol Biol Phys*, 2022. [3].

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- Open-label, phase II trial included 96 patients randomised 1:1 to receive NTG plus WBRT (30Gy/10 fractions) or WBRT alone.
- 55.3% of the control group had *EGFR*-mutated tumours and 44.7% of the NTG group.
- The primary endpoint of intracranial objective response rate (iORR), evaluated at 3 months, was met with the NTG group demonstrating a significantly higher iORR compared to control (56.6% vs. 32.7%,  $p = 0.024$ ).
- Intracranial progression-free survival, a secondary endpoint, was also significantly longer in the NTG group (27.7 vs 9.6 months; HR 0.47 [95% CI: 0.24–0.89];  $p = 0.021$ ) but there was no difference in overall survival.
- On further analysis, patients with *EGFR*-mutated disease were found to have the greatest benefit from the addition of NTG.
- The patients in the NTG group did report a significantly higher rate of vomiting ( $p = 0.016$ ) however.

#### 4. Evidence supports the use of Olaparib and Rucaparib in BRCA-mutated metastatic castrate-resistant prostate cancer (mCRPC). Can Niraparib join the group?

*Niraparib in patients with metastatic castration-resistant prostate cancer and DNA repair gene defects (GALAHAD): a multicentre, open-label, phase 2 trial.* Smith. M.R. et al. *Lancet Oncol*, 2022 [4].

- Open label, single arm, phase II trial. Patients with mCRPC who had progressed following treatment with a taxane and an androgen signalling inhibitor and had a confirmed DNA repair gene defect (DRD). All received oral Niraparib 300mg daily but were stratified according to *BRCA* mutational status.
- Median treatment time was 6.5 months in *BRCA*-mutated group and 3.6 months in non-*BRCA* group.

- Primary end point of objective response was met in 26 of 76 *BRCA*-mutated cohort (34.2%, 95% CI 23.7–46.0). Median duration of objective response was 5.5 months (95% CI 3.91–7.20). Objective response was seen in 5 out of 47 of the non-*BRCA* cohort (10.6%, 95% CI 3.5–23.1).
- 2-year event free survival in the *BRCA* cohort was 15.2% (95% CI 7.7–25.1).
- Anti-tumour activity of Niraparib in the *BRCA* cohort is established with a tolerable safety profile.

## Conflicts of interest

The authors declare no conflict of interest

## References

- [1] Andreyev HJN, Matthews J, Adams C, Gothard L, Lucy C, Tovey H, et al. Randomised single centre double-blind placebo controlled phase II trial of Tocovid SupraBio in combination with pentoxifylline in patients suffering long-term gastrointestinal adverse effects of radiotherapy for pelvic cancer: The PPALM study. *Radiother Oncol* 2022;168:130–137. <https://doi.org/10.1016/j.radonc.2022.01.024>.
- [2] Nichols AC, Theurer J, Prisman E, Read N, Berthelet E, Tran E, et al. Randomized Trial of Radiotherapy Versus Transoral Robotic Surgery for Oropharyngeal Squamous Cell Carcinoma: Long-Term Results of the ORATOR Trial. *J Clin Oncol* 2022 Mar 10;40(8):866–875. <https://doi.org/10.1200/JCO.21.01961>.
- [3] Arrieta O, Hernández-Pedro N, Maldonado F, Ramos-Ramírez M, Yamamoto-Ramos M, López-Macías D, et al. Nitroglycerin plus whole intracranial radiotherapy for brain metastases in non-small cell lung cancer patients: A randomized, open-label, phase II clinical trial. *Int J Radiat Oncol* 2022. <https://doi.org/10.1016/j.ijrobp.2022.02.010>.
- [4] Smith MR, Scher HI, Sandhu S, Efstathiou E, Lara Jr PN, Yu EY, et al. Niraparib in patients with metastatic castration-resistant prostate cancer and DNA repair gene defects (GALAHAD): a multicentre, open-label, phase 2 trial. *Lancet Oncol* 2022 Mar;23(3):362–373. [https://doi.org/10.1016/S1470-2045\(21\)00757-9](https://doi.org/10.1016/S1470-2045(21)00757-9).