



OncoFlash – Research Updates in a Flash! (March 2022 Edition)



C. Crockett ^{*1}, C. Lorimer ^{†1}

^{*}The Christie NHS Foundation Trust, Manchester, UK

[†]University Hospitals Sussex NHS Foundation Trust, WSX, UK

Does the effect of adjuvant olaparib extend beyond the 2-year treatment period in BRCA-mutated advanced ovarian cancer?

Maintenance olaparib for patients with newly diagnosed advanced ovarian cancer and a BRCA mutation (SOLO1/GOG 3004): 5-year follow-up of a randomised, double-blind, placebo-controlled, phase 3 trial. Banerjee, S. et al. *Lancet Oncol* 2021. [1].

- 260 patients with stage III (debulked) or stage IV ovarian cancer with a BRCA mutation, who had responded to platinum-based chemotherapy without the addition of bevacizumab, randomised to olaparib or placebo for two years.
- Allowed to continue treatment if residual disease at two years (only 13 patients).
- 5-year adhoc progression-free survival (PFS) data published.
- Median PFS was 56 months (95% CI 41.9-not reached) with olaparib versus (vs.) 13.8 months (11.1–18.2) with placebo (HR 0.33 [95% CI 0.25–0.43]) without any detriment to quality of life.
- Benefit seen irrespective of stage of cancer and BRCA 1 vs. 2 mutation and extends beyond treatment period.
- SOLO-2 reported a much lower PFS of only 19.1 months with olaparib in relapsed ovarian cancer leading the authors to stress the importance of the early use of PARP inhibitors in the treatment pathway.

Could 4-dimensional computed tomography (4DCT) ventilation functional avoidance RT reduce the rate of pneumonitis in patients receiving treatment for lung cancer?

Results of a Multi-institutional Phase 2 Clinical Trial for 4DCT-ventilation Functional Avoidance Thoracic Radiation Therapy. Vinogradskiy, Y et al. *Int J Radiat Oncol Biol Phys* 2021. [2].

- Prospective study including 67 lung cancer patients who received curative-intent thoracic RT and chemotherapy.
- 4DCT scans were used to generate 4DCT-ventilation images which in turn were used to generate functional lung tissue avoidance plans with the aim of reducing the volume of functional lung irradiated but maintaining adequate dose to tumour.
- The study hypothesis was that functional avoidance RT could reduce the rate of grade ≥ 2 pneumonitis to 12% from 25% (historical control pneumonitis rate based on a pooled comparator of previous studies).
- A predefined cut off to define trial positivity was set at grade ≥ 2 pneumonitis $\leq 16.4\%$.
- Patients were assessed by a clinician at 3-, 6- and 12-months following RT for symptoms relating to pneumonitis.
- Median RT prescription dose was 60Gy (range 45–66Gy) delivered in 30 fractions (range 15–33).
- Mean reduction in functional lung volume receiving ≥ 20 Gy as a result of functional avoidance was 3.5% (range 0–12.8%).
- After a median follow-up of 312 days, the rate of grade ≥ 2 pneumonitis was 14.9%.
- Authors conclude there is a potential benefit of functional avoidance RT and a need to evaluate it further in a phase III trial.

Author for correspondence: Cathryn Crockett

E-mail addresses: Cathryn.crockett@nhs.net, cressida.lorimer@nhs.net (C. Crockett).

¹ Both authors contributed equally to this work.

<https://doi.org/10.1016/j.clon.2022.01.011>

0936-6555/© 2022 Published by Elsevier Ltd on behalf of The Royal College of Radiologists.

Does the addition of temozolomide (TMZ) chemotherapy improve outcomes for patients with stage II/III isocitrate dehydrogenase wild-type (IDH-wt) and telomerase reverse-transcriptase promoter mutation (TERTp-mut) diffuse glioma treated with radiotherapy (RT)?

Chemoradiotherapy with temozolomide vs. radiotherapy alone in patients with IDH wild-type and TERT promoter mutation WHO grade II/III gliomas: A prospective randomized study. Qui, X *et al.* *Radiother and Oncol* 2022. [3].

- Patients with stage II/III IDH-wt and TERTp-mut diffuse glioma are known to have poorer outcomes and their optimal management has not yet been determined.
- Prospective study of 37 patients randomised to receive RT alone (n = 18, 60Gy in 30 fractions delivered once daily over five weeks) vs. RT plus concurrent TMZ (75mg/m² daily) and adjuvant TMZ (n = 19).
- Median overall survival (OS) was significantly higher with the addition of TMZ compared to RT alone (25 vs. 17 months, respectively; HR 0.271 [95% CI 0.092–0.793]; *p* = 0.017).
- PFS also appeared improved with TMZ but not significantly (16 vs. 7 months; HR, 0.917 [95% CI 0.397–2.120]; *p* = 0.840).
- On multivariate analysis both TMZ use, and female sex were associated with significantly improved OS (*p* = 0.001, *p* = 0.016, respectively).

Dose escalated radiotherapy in locally advanced oesophageal cancer – is there any benefit?

Randomized Study on Dose Escalation in Definitive Chemoradiation for Patients With Locally Advanced Esophageal

Cancer (ARTDECO Study). Hulshof, M *et al.* *J Clin Oncol* 2021. [4].

- Radiotherapy dose escalation study in patients with T1-4 N0-3 M0-1 (involved SCF nodes) oesophageal or gastro-oesophageal junction adeno- or squamous cell carcinomas.
- Patients randomised to concurrent chemoradiotherapy consisting of 50.4Gy in 28 fractions or 61.6Gy in 28 fractions, with a simultaneous integrated boost (SIB) to the primary tumour, alongside carboplatin and paclitaxel chemotherapy.
- No difference in 3-year locoregional PFS of 53% (95% CI 43 to 64) in the standard arm versus 59% (95% CI 49 to 70) in the SIB arm (*p* = 0.24).
- No difference in 3-year OS of 42% (95% CI 34 to 52) in the standard arm and 39% (95% CI 31 to 49) in the SIB arm (*p* = 0.22).
- Authors conclude there is no evidence to support dose escalation above 50.4Gy.

References

- [1] Banerjee S, Moore KN, Colombo N, Scambia G, Kim BG, Oaknin A, *et al.* Maintenance olaparib for patients with newly diagnosed advanced ovarian cancer and a BRCA mutation (SOLO1/GOG 3004): 5-year follow-up of a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2021 Dec; 22(12):1721–1731. [https://doi.org/10.1016/S1470-2045\(21\)00531-3](https://doi.org/10.1016/S1470-2045(21)00531-3).
- [2] Vinogradskiy Y, Castillo R, Castillo E, Schubert L, Jones BL, Faught A, *et al.* Results of a Multi-institutional Phase 2 Clinical Trial for 4DCT-ventilation Functional Avoidance Thoracic Radiation Therapy. *Int J Radiat Oncol Biol Phys (online)* 2021 Nov. <https://doi.org/10.1016/j.ijrobp.2021.10.147>.
- [3] Qiu X, Chen Y, Bao Z, Chen L, Jiang T. Chemoradiotherapy with temozolomide vs. radiotherapy alone in patients with IDH wild-type and TERT promoter mutation WHO grade II/III gliomas: A prospective randomized study. *Radiother Oncol* 2022 Feb;167:P1–P6. <https://doi.org/10.1016/j.radonc.2021.12.009>.
- [4] Hulshof M, Geijsen ED, Rozema T, Oppedijk V, Buijsen J, Neelis KJ, *et al.* Randomized study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer (ARTDECO study). *J Clin Oncol* 2021 Sep 1; 39(25):2816–2824. <https://doi.org/10.1200/JCO.20.03697>.