8LB Late Breaking

# Chemotherapy choices and doses in frail and elderly patients with advanced colorectal cancer: an MRC randomised clinical trial (FOCUS2)

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**Background:** Frail elderly patients, though commonly treated, are under-represented in trials. Evidence is needed to guide drug choices and doses in this population.

**Methods:** FOCUS2 is a multicenter, 2×2 factorial trial in patients with unpretreated metastatic colorectal cancer, unfit for full-dose combination therapy. Physical, mental, comorbidity and QL status were assessed at baseline. Randomisation was to (A) infusional fluorouracil (FU); (B) oxaliplatin plus FU (OxFU); (C) capecitabine (Cap); or (D) OxCap. Standard regimens were used, but starting at 80% standard doses. Patients were considered for dose-increase to 100% after 6 wks, with full health/QL and tumour reassessment after 12 wks. Two factorial questions were asked: (AB v CD) – does replacing FU with Cap improve QL? (1º endpoint: improved QL at 12 wk); and (AC v BD) – what benefit is Ox in this population? (1º endpoint: PFS). Baseline factors were assessed as potential predictors of treatment outcome using a composite scale (good; intermediate; poor) incorporating response, toxicity/AEs, and patient views.

**Results:** 459 patients were randomised. 43% were aged over 75 yr, 35% 70–75 yr, 22% under 70 yr; 29% were performance status 2, 49% PS1, 22% PS0. Outcomes are presented in the table.

| Outcomes | A FU | B OxFU | C Cap | D OxCap | AB v CD (FU v Cap) | AC v BD (± Ox) |
|---|---|---|---|---|---|---|
| PFS hazard ratio (n = 459) | | | | | HR = 1.03, p = 0.7650 | HR = 0.88, p = 0.1794 |
| RR by wk 12 (n = 364) | 15% | 42% | 15% | 39% | p = 0.641 | **p < 0.0001** |
| Dose increased at wk 6 | 50% | 36% | 41% | 31% | p = 0.09 | **p = 0.01** |
| Any gr ⩾3 tox in 1st 12 wks | 24% | 29% | 37% | 41% | **p = 0.006** | p = 0.264 |
| 60-d all-cause mortality | 16% | 4% | 9% | 10% | p = 0.862 | p = 0.097 |
| Improved QL at 12 wks (n = 246) | 59% | 51% | 64% | 47% | p = 0.887 | **p = 0.043** |
| Improved EQ5D score (n = 263) | 60% | 75% | 61% | 62% | p = 0.334 | p = 0.189 |
| Improved ADL score (n = 179) | 54% | 51% | 37% | 40% | **p = 0.05** | p = 0.99 |

In univariate analysis, pre-treatment factors correlating with good or poor treatment outcome included: nausea/vomiting and pain score (both $p < 0.001$); nutritional score and fatigue (both $p < 0.005$); EQ5D score, number of disease sites and liver-only disease (all $p < 0.01$); dyspnoea and raised WBC ($p < 0.05$). Multivariate logistic regression analyses are being performed on these data.

**Conclusions:** The strategy of starting at 80% standard doses with escalation at 6 weeks appears successful in limiting toxicity. In this population, substituting capecitabine for FU increase rates of grade ⩾3 toxicity and did not improve QL. Adding oxaliplatin increased the response rate but had only a non-significant effect on PFS. Further analysis of prediction of outcomes from baseline assessment data will be presented.