**128P Erythromycin readthrough of APC nonsense stop codon mutation in Familial adenomatous polyposis**

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**Background:** Read-through of genetic nonsense mutations has been proven effective in mice models and for some human clinical conditions and can lead to the expression of a full-length protein. Based on initial work that showed aminoglycoside and macrolide antibiotics can read-through adenomatous polyposis coli (APC) nonsense mutations, we have initiated a clinical trial for erythromycin treatment in familial polyposis (FAP) patients that result from nonsense mutations in the APC gene.

**Methods:** A prospective, open label intervention study with oral erythromycin 250mg BID for 4 months. The study included a baseline and post-treatment colonoscopies at 4 and 12 months, in which a polyp count and measurements were conducted. Polyps were analyzed for Wnt target gene expression. Repeated measures ANOVA was used for the comparison of polyp number and size across repeated measurements. Annual rate of changes in polyp number and size were compared pre and post intervention using the dependent samples t test.

**Results:** We recruited 9 patients, 5 completed 12 months of follow up. Polyp number at baseline, after 4 and 12 months were 37.0±31.7, 33.6±38.6 and 30.8±36.7, respectively (0.099 between subject effect) and polyp maximal size 7.0±1.4, 6.3±2.1 and 4.1±1.0 (<0.001 between subject effect). Mean pre and post treatment (4 months) values for 9 patients were 73.7±13.9 and 36.3±23.0 for KI67; 38.1±72.6 and 16.2±24.3 for CYCLIN D; 16.8±23.9 and 6.1±7.0 for AXIN; 2.6±6.0 to 0.08±0.06 for CYCLIN D. The individual rate of polyp number and maximal size change according to the change between 1 year pre-study to study baseline colonoscopies was compared with the rate between baseline and 12 months post study results. Polyp number change was 33.8±77.2% before and -38.7±23.5% after (p = 0.125) and for polyp maximal size: 33.8±77.7% and -38.7±23.5% (p = 0.125).

**Conclusions:** In this pilot study, initial results point to molecular and clinical effects of erythromycin, which indicate that APC read-through is feasible in FAP and requires further study.

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