Modulo richiesta assegno

TUTOR	**Luigi Ricciardiello**	
Fascia VRA	(compilazione a cura della Giunta)	*Punti*
PRODUZIONE SCIENTIFICA ASSEGNISTI NELL'ULTIMO QUADRIENNIO		*Punti*
Nome e n° mesi assegnista 1	**Anna Prossomariti (60 mesi – Chiuso)**	
Produzione scientifica in extenso su riviste indicizzate PubMed	1. **Prossomariti A**, Piazzi G, Alquati C, Ricciardiello L. Are Wnt/β-Catenin and PI3K/AKT/mTORC1 Distinct Pathways in Colorectal Cancer? Cell Mol Gastroenterol Hepatol 2020;10(3):491-506. 2. Piazzi G, **Prossomariti A**, Baldassarre M, Montagna C, Vitaglione P, Fogliano V, Biagi E, Candela M, Brigidi P, Balbi T, Munarini A, Belluzzi A, Pariali M, Bazzoli F, Ricciardiello L.A Mediterranean Diet Mix Has Chemopreventive Effects in a Murine Model of Colorectal Cancer Modulating Apoptosis and the Gut Microbiota. Front Oncol. 2019 Mar 12;9:140. 3. **Prossomariti A**, Piazzi G, D'Angelo L, Miccoli S, Turchetti D, Alquati C, Montagna C, Bazzoli F, Ricciardiello L. miR-155 Is Downregulated in Familial Adenomatous Polyposis and Modulates WNT Signaling by Targeting AXIN1 and TCF4. Mol Cancer Res. 2018 Aug 2. doi: 10.1158/1541-7786.MCR-18-0115. 4. **Prossomariti A**, Sokol H, Ricciardiello L. Nucleotide-Binding Domain Leucine-Rich Repeat Containing Proteins and Intestinal Microbiota: Pivotal Players in Colitis and Colitis-Associated Cancer Development. Front Immunol. 2018 May 14;9:1039. doi: 10.3389/fimmu.2018.01039. eCollection 2018. 5. Ciavarella M, Miccoli S, **Prossomariti A**, Pippucci T, Bonora E, Buscherini F, Palombo F, Zuntini R, Balbi T, Ceccarelli C, Bazzoli F, Ricciardiello L, Turchetti D and Piazzi G. Somatic APC mosaicism and oligogenic inheritance in genetically unsolved colorectal adenomatous polyposis patients. Eur J Hum Genet. 2018 Mar;26(3):387-395. doi: 10.1038/s41431-017-0086-y.	
Nome e n° mesi assegnista 2	**Chiara Alquati (31 mesi – attivo)**	
Produzione scientifica in extenso su riviste	1. **Alquati C**, Prossomariti A, Piazzi G, Buttitta F, Bazzoli F, Laghi L, Ricciardiello L. Discovering the Mutational Profile of Early Colorectal Lesions: A Translational	

indicizzate PubMed	Impact. Cancers (Basel). 2021 Apr 25;13(9):2081. doi: 10.3390/cancers13092081. 2. Prossomariti A, Piazzi G, **Alquati C**, Ricciardiello L. Are Wnt/β-Catenin and PI3K/AKT/mTORC1 Distinct Pathways in Colorectal Cancer? Cell Mol Gastroenterol Hepatol 2020;10(3):491-506. 3. Prossomariti A, Piazzi G, D'Angelo L, Miccoli S, Turchetti D, **Alquati C**, Montagna C, Bazzoli F, Ricciardiello L. miR-155 Is Downregulated in Familial Adenomatous Polyposis and Modulates WNT Signaling by Targeting AXIN1 and TCF4. Mol Cancer Res. 2018 Aug 2. doi: 10.1158/1541-7786.MCR-18-0115.
Nome e n° mesi assegnista 3	**Francesco Buttitta (23 mesi – attivo)**
Produzione scientifica in extenso su riviste indicizzate PubMed	1. Aelvoet AS, Buttitta F, **Ricciardiello L**, Dekker E. Management of familial adenomatous polyposis and MUTYH-associated polyposis; new insights. Best Pract Res Clin Gastroenterol. 2022 Jun-Aug;58-59:101793. 2. Montale A, **Buttitta F**, Pierantoni C, Ferrari C, Cameletti M, Colussi D, Miccoli S, Bazzoli F, Turchetti D, Ricciardiello L. Chromoendoscopy is not superior to white light endoscopy in improving adenoma detection in Lynch Syndrome cohort undergoing surveillance with high-resolution colonoscopy: a real-world evidence study. Dig Dis. 2021 Aug 24. doi: 10.1159/000518840. Online ahead of print.PMID: 34515093 No abstract available. 3. Alquati C, Prossomariti A, Piazzi G, **Buttitta F**, Bazzoli F, Laghi L, Ricciardiello L. Discovering the Mutational Profile of Early Colorectal Lesions: A Translational Impact. Cancers (Basel). 2021 Apr 25;13(9):2081. doi: 10.3390/cancers13092081.PMID: 33923068 4. Buscarini E, Benedetti A, Monica F, Pasquale L, **Buttitta F**, Cameletti M, Ferrari C, Ricciardiello L; FISMAD: the FISMAD-ALERT Survey Group. Changes in digestive cancer diagnosis during the SARS-CoV-2 pandemic in Italy: A nationwide survey. Dig Liver Dis. 2021 Jun;53(6):682-688. doi: 10.1016/j.dld.2021.02.021. Epub 2021 Mar 8. 5. Vanella G, Capurso G, Burti C, Fanti L, Ricciardiello L, Souza Lino A, Boskoski I, Bronswijk M, Tyberg A, Krishna Kumar Nair G, Angeletti S, Mauro A, Zingone F, Oppong KW, de la Iglesia-Garcia D, Pouillon L, Papanikolaou IS, Fracasso P, Ciceri F, Rovere-Querini P, Tomba C, Viale E, Eusebi LH, Riccioni ME, van der Merwe S, Shahid H, Sarkar A, Yoo JWG, Dilaghi E, Speight RA, Azzolini F, **Buttitta F**, Porcari S, Petrone MC, Iglesias-Garcia J, Savarino EV, Di Sabatino A,

	Di Giulio E, Farrell JJ, Kahaleh M, Roelandt P, Costamagna G, Artifon ELA, Bazzoli F, Testoni PA, Greco S, Arcidiacono PG. Gastrointestinal mucosal damage in patients with COVID-19 undergoing endoscopy: an international multicentre study.BMJ Open Gastroenterol. 2021 Feb;8(1):e000578. doi: 10.1136/bmjgast-2020-000578.PMID: 33627313 6. Ricciardiello L, Ferrari C, Cameletti M, Gaianill F, **Buttitta F**, Bazzoli F, Luigi de'Angelis G, Malesci A, Laghi L. Impact of SARS-CoV-2 Pandemic on Colorectal Cancer Screening Delay: Effect on Stage Shift and Increased Mortality. Clin Gastroenterol Hepatol. 2021 Jul;19(7):1410-1417.e9. doi: 10.1016/j.cgh.2020.09.008. Epub 2020 Sep 6.
Nome e n° mesi assegnista 4	**Giulia Piazzi (52 mesi – Dal 2013 Titolare di progetto giovani Ricercatori Regione ER) Completato**
Produzione scientifica in extenso su riviste indicizzate PubMed	1. Prossomariti A, **Piazzi G**, Alquati C, Ricciardiello L. Are Wnt/β-Catenin and PI3K/AKT/mTORC1 Distinct Pathways in Colorectal Cancer? Cell Mol Gastroenterol Hepatol 2020;10(3):491-506. 2. **Piazzi G**, Prossomariti A, Baldassarre M, Montagna C, Vitaglione P, Fogliano V, Biagi E, Candela M, Brigidi P, Balbi T, Munarini A, Belluzzi A, Pariali M, Bazzoli F, Ricciardiello L.A Mediterranean Diet Mix Has Chemopreventive Effects in a Murine Model of Colorectal Cancer Modulating Apoptosis and the Gut Microbiota. Front Oncol. 2019 Mar 12;9:140. 3. Prossomariti A, **Piazzi G**, D'Angelo L, Miccoli S, Turchetti D, Alquati C, Montagna C, Bazzoli F, Ricciardiello L. miR-155 Is Downregulated in Familial Adenomatous Polyposis and Modulates WNT Signaling by Targeting AXIN1 and TCF4. Mol Cancer Res. 2018 Aug 2. doi: 10.1158/1541-7786.MCR-18-0115. 4. Ciavarella M, Miccoli S, Prossomariti A, Pippucci T, Bonora E, Buscherini F, Palombo F, Zuntini R, Balbi T, Ceccarelli C, Bazzoli F, Ricciardiello L, Turchetti D and **Piazzi G**. Somatic APC mosaicism and oligogenic inheritance in genetically unsolved colorectal adenomatous polyposis patients. Eur J Hum Genet. 2018 Mar;26(3):387-395. doi: 10.1038/s41431-017-0086-y.
Nome e N° mesi Assegnista 5	**Dr. Sartini Alessandro (12 mesi Autofinanziato terminato anticipatamente)**
Produzione scientifica in extenso su riviste indicizzate PubMed	1. **Sartini A**, Scaioli E, Liverani E, Bellanova M, Ricciardiello L, Bazzoli F, Belluzzi A. Retention Rate, Persistence and Safety of Adalimumab in Inflammatory Bowel Disease: A Real-Life, 9-Year, Single-Center

	Experience in Italy. Dig Dis Sci. 2018 Oct 17. doi: 10.1007/s10620-018-5329-4. [Epub ahead of print] PubMed PMID: 30334112.

TITOLO DEL PROGETTO			
STUDIO CLINICO RANDOMIZZATO CONTROLLATO IN DOPPIO CIECO SULL'EFFETTO, LA TOLLERABILITA' E LA SICUREZZA DELL'ACIDO EICOSAPENTAENOICO COME ACIDO GRASSO LIBERO IN PAZIENTI AFFETTI DA POLIPOSI ADENOMATOSA FAMILIARE			
ASSEGNO FINANZIATO DA PROGETTO COMPETITIVO *(barrare la casella corrispondente)*	☐ SI	X NO	*Punti*
SE IL FINANZIAMENTO È COMPETITIVO L'ENTE FINANZIATORE			
PROGETTO/ATTIVITÀ A SCOPO COMMERCIALE *(es. sperimentazione profit)*	☐SI	X NO	
CARATTERISTICHE DEL PROGETTO (*biomedico/osservazionale/clinico-interventistico/multidisciplinare*)	Biomedico		
STATO DI APPROVAZIONE DEL PROGETTO DA PARTE DEL COMITATO ETICO (*se necessario per il tipo di studio barrare o evidenziare la casella corrispondente*)	X Ottenuto	☐ Da ottenere	

DESCRIZIONE DEL PROGETTO *(max 800 parole)*	*Punti*

Stato dell'Arte e Razionale

Familial Adenomatous Polyposis (FAP) is an inherited susceptibility to diffuse colorectal adenomas and colorectal carcinoma, occurring in close to 100% of unresected colons, and caused by a germline mutation in the APC gene located on the long arm of chromosome 5 (Kinzler et al 1996). To prevent cancer development, it is recommended that patients with FAP undergo colectomy with ileo-anal or ileo-rectal anastomosis (or colectomy and end-ileostomy) at a socially convenient time before polyp progression to malignancy and before the age of 25. Patients with the attenuated FAP phenotype, often associated with mutations at the 5' terminus (exon 4 and proximally) (Spiro et al 1993), have fewer polyps and may often delay colectomy. It has been suggested that omega-3 PUFAs in fish oil can modulate the high levels of colonic mucosal cell proliferation rates associated with sporadic colonic adenomas (Anti M et al 1994) and furthermore, work at St George's Hospital Medical School, London, has shown significant beneficial effects of cell proliferation and apoptosis rates on the colonic mucosa of patients with a history of colonic adenomas using a highly purified, form of EPA as the free fatty acid (Courtney et al 2005). The effects of EPA-FFA on polyps have been investigated in the Multiple intestinal neoplasia (Min) mouse. The Min mouse has a mutation of the tumour suppressor gene (APC). This confers a predisposition to form polyps in the small and large intestines which develop rapidly within the first 12 weeks of life. Compared to Ctrl, EPA-FFA 2.5% and 5% dramatically repressed polyp formation (by 71.5% and 78.6%, respectively, $P < 0.0001$) and reduced polyp load (by 82.5% and 93.4%, respectively, $P < 0.0001$). A

chemoprevention trial in FAP patients has been conducted using the EPA-FFA gastro resistant capsules. Consenting subjects, aged 18 or older, with a diagnosis of FAP and an evaluable rectal segment having 3 or more rectal polyps ≥2mm in size (within an area of the rectum that could be tattooed) were recruited. Subjects satisfying the entry criteria were randomised (1:1) to receive one of two treatments: placebo twice daily or 500mg EPA, as the free fatty acid, twice daily (total daily dose 2g) for 6 months. In total, 58 subjects were randomised, 29 to the placebo group and 29 to the EPA treatment group. The study demonstrated a statistically significant reduction in number of polyps (p=0.0046 Full analysis set) in a focal area of the rectum following six months treatment with EPA compared to placebo. Statistically significant differences between the EPA treatment group and placebo group were found for percentage change in number of polyps, percentage change in total polyp diameter and global rectal polyp burden (as assessed by the expert review panel).

Ipotesi e obiettivi

Supplementation of EPA-FFA is superior compared to placebo in reducing the number of total polypectomies in patients with FAP at 24 months.

Metodi

This is a randomised, double-blind, placebo-controlled, multicenter study to be conducted across Europe with an expected study duration of 2 years and 1.5 months to determine the safety and efficacy of EPA-FFA gastro-resistant capsules. Subjects known to have a diagnosis of FAP, and attending a specialist clinic, will be contacted. Eligible subjects will provide written informed consent prior to any study specific procedures being conducted. Subjects with confirmed diagnosis of FAP, compliance with the inclusion and exclusion criteria and providing written informed consent will be registered on the e-CRF to obtain a screening number.

Subjects will then undergo an endoscopy. A video record will be made of the endoscopic examination of the rectum which will be viewed in a spiral fashion to the anal verge. All polyps of > 5mm in the rectum will be removed where possible, a record will be made of the size, rationale for removal and location of any polyps prior to their removal, this is conducted after completion of the video record of the endoscopic examination. Polyps ≤ 5mm in the rectum should be left in place unless there are other clinical reasons deemed necessary for these to be removed in which case the rationale for removal should be documented. The subjects FAP will be classified in accordance with the IPSS. The IPSS classification will be verified by the Polyp Video Scoring committee prior to randomisation. Subjects will then undergo an EGD. The duodenal adenomas will be classified according to the Spigelman classification. Subjects compliance with the inclusion and exclusion criteria will be re-evaluated following endoscopy and eligible subjects will be randomised.

Eligible subjects will be randomised on a 1:1 basis to one of the two treatment arms: EPA-FFA 500mg gastro-resistant capsules or matching Placebo gastro-resistant capsules.

Subjects will be provided with a supply of investigational medicinal product (IMP). Following the baseline visit subjects will administer IMP orally two capsules twice daily.

Visit Procedures (6 months, 12 months, 18 months):

Subjects will attend the clinic every 6 months.

Subjects will then undergo an endoscopy. A video record will be made of the endoscopic examination of the rectum which will be viewed in a spiral fashion to the anal verge. All polyps of > 5mm in the rectum will be removed where possible, a record will be made of the size, rationale for removal and location of any polyps prior to their removal, this is conducted after completion of the video record of the endoscopic examination. Polyps ≤ 5mm in the rectum should be left in place

unless there are other clinical reasons deemed necessary for these to be removed in which case the rationale for removal should be documented. 24 months Visit Procedures:
Subjects will attend the clinic and the diary will be reviewed to ensure completion of the diary and to check for any changes in their condition or concomitant medication. Any changes in health and concomitant medications must be registered in the e-CRF. Subjects will then undergo an endoscopy. A video record will be made of the endoscopic examination of the rectum which will be viewed in a spiral fashion to the anal verge. All polyps of > 5mm in the rectum will be removed where possible, a record will be made of the size, rationale for removal and location of any polyps prior to their removal, this is conducted after completion of the video record of the endoscopic examination. Polyps ≤ 5mm in the rectum should be left in place unless there are other clinical reasons deemed necessary for these to be removed in which case the rationale for removal should be documented. Subjects will then undergo an EGD. The duodenal adenomas will be classified according to the Spigelman classification.
Of the 208 foreseen patients, the consortium has enrolled 110 patients so far Europewide.

Risultati attesi
Over a 24 months period of treatment EPA-FFA reduces significantly the number of total polypectomies compared to placebo (for all statistical description please refer to the clinical trial protocol).

DESCRIZIONE DELLE ATTIVITÀ DELL'ASSEGNISTA (Description of the expected research activities) *(per i **nuovi** assegni: max 400 parole; competenze richieste, scansione temporale della formazione, scansione temporale dell'attività, obiettivi primari e secondari)* *(per i **rinnovi**: max 600 parole – da integrare con la relazione dell'assegnista; formazione raggiunta, attività effettuata, obiettivi raggiunti/competenze acquisite, formazione ancora da acquisire (se pertinente), scansione temporale dell'attività durante il rinnovo)*	*Punti*

Il candidato vincitore dovrà possedere una laurea in medicina e chirurgia.
Altre competenze/requisiti richieste ai candidati:
Il canditato dovrà avere dimostrato esperienza acquisita legata ad attività di gestione di trial clinici.
In particolare: il candidato vincitore dovrà coadiuvare il PI nell'arruolamento e gestione dei pazienti con FAP potenzialmente arruolabili oltre a gestire i dati relativi al trial.

Il candidato vincitore, dovrà svolgere le seguenti attività:

1) Coadiuvare il PI nella selezione dei pazienti
2) Coadiuvare il PI nella gestione del trial clinico e dei dati ottenuti. Coadiuvare il PI nella gestione del monitoraggio dello studio con la CRO coinvolta.
3) Dovrà essere coinvolto nella gestione e revision dei video che verranno ottenuti da tutti I centri internazionali coinvolti nei trials. Per il periodo del trial verranno generati circa 1200 video che dovranno essere editati e caricati su piattaforma criptata dedicata per lo scoring da parte di un blinded review panel. Gestione video per valutazione da parte del video panel review.

Scansione Temporale
Primo semestre: Selezione dei pazienti da arruolare per completare lo studio. Gestione video dei centri nazionali e internazionali.
Secondo Semestre: completare arruolamento dei pazienti e campionamento bioptico. Gestione dei

video dai centri nazionali e internazionali.

SE RINNOVO, SI RICORDA DI ALLEGARE ANCHE LA RELAZIONE DELL'ASSEGNISTA.

Scheda attività assistenziale (se prevista)

ATTIVITÀ / N. ORE SETTIMANA
AZIENDA SANITARIA PRESSO CUI SI SVOLGERÀ L'ATTIVITÀ

Si ricorda che, come previsto dagli Accordi sull'impiego nell'attività assistenziale dei Titolari di assegni di ricerca, sottoscritti tra l'Università di Bologna e le Aziende Ospedaliere di riferimento, una volta stipulato il contratto con il vincitore della selezione, il tutor deve consegnare alla Direzione Medica Ospedaliera la relativa modulistica, nella quale andranno riportate le attività qui segnalate.