

Welcome to the International Rare Cancers Initiative newsletter, October 2018

The International Rare Cancers Initiative was set up in 2011 to facilitate the development and delivery of hypothesis driven, interventional clinical trials for patients with rare cancers. The initiative to date has convened working groups looking at twelve rare cancer types and opened seven trials, as well as stimulating a number of other publications on rare cancers.

In this issue of the newsletter:

- New working groups expand the reach of IRCI
- Updates from IRCI Working Groups
- IRCI publication list

New working groups expand the reach of IRCI

Earlier this year, IRCI ran its second expression of interest (EOI) call for new working groups wishing to develop an international trial in a rare cancer. It was encouraging to see a high degree of interest from the international community, with 24 applications received. All the participating countries in IRCI had at least one lead applicant from their country submit an EOI, showing this initiative has true global reach and interest.

We are pleased to have been able to support 10 of the applications made, using our resource creatively to give the maximum number of opportunities to applicants, as well as ensuring that skills and ideas can be shared among researchers focusing on similar disease types. As such, two new working groups were formed covering 5 of the applicants, and 5 additional applications were supported in other ways.



24 applications received

10 applications supported



Multiple collaborators

Supported applications

Rare Haematological Tumours: From the 10 applications that were supported, 2 applicants had shown a strong interest in forming a group within Rare Haematological Tumours. Areas of interest that the applicants wish to explore further and are keen to progress towards a viable study include angioimmunoblastic T-cell lymphoma and malignant histiocytosis.

Rare Genitourinary Tumours: 3 further applicants out of the 10 were supported in creating a new group within Rare Genitourinary Tumours. All 3 applicants had shown a key interest within this space and areas to be explored include urological cancers; transitional cell carcinoma of the bladder and urinary tract; and upper tract urothelial carcinoma.

An additional 3 applications were supported in ways such that they were invited to merge with existing working groups with 1 application holding an initial 1-day meeting space to discuss a trial concept in synovial sarcoma.

The remaining 1 application received was in cutaneous lymphoma where the applicants were invited to merge into the existing working group for Merkel Cell Carcinoma to become the IRCI Rare Skin Cancer working group.

NEW Rare Genitourinary Tumours Group	Relapsed/ Metastatic Anal Cancer Group
NEW Rare Haematological Tumours Group	Rare Melanoma Group
Rare Skin Cancer Group	Small Bowel Adenocarcinoma Group
Gynaecological Sarcoma Group	Salivary Gland Cancer Group
	Penile Cancer Group

Next steps

Newly established groups will have the opportunity to have an orientation call to seek further input on the initiative and to learn more on how IRCI operates. Meeting spaces will be allocated to the working groups at ASCO each year at which to discuss memberships and trial concept. Groups will be facilitated for up to three years, at which time it would be anticipated that trial set-up would be under way.

You can follow IRCI's activities on the website at www.irci.info, or contact the IRCI secretariat at irci@cancer.org.uk

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Updates from IRCI Working Groups



IRCI Gynaecological Sarcoma Group

HGUS: A randomized phase II study evaluating the role of maintenance therapy with cabozantinib vs placebo in High Grade Uterine Sarcoma (HGUS) after stabilization or response to CT following surgery or in metastatic 1st-line treatment (**IRCI 006**)

- Chief Investigator: Prof Isabelle Ray-Coquard (Léon Bérard Cancer Centre, France)
- Lead coordinating centre: EORTC HQ
- 18/54 patients have now been recruited across 11 sites in 7 countries.
- The trial is open in Belgium, the Netherlands, Germany, France, Spain and Italy; the UK plans to open 6 sites.
- The trial has been amended to include all high-grade uterine sarcomas, following closure of the uLMS study.

uLMS: A phase III randomised trial of gemcitabine plus docetaxel followed by doxorubicin versus observation for uterus-limited, high grade uterine leiomyosarcoma

- Chief Investigator: Dr Martee Hensley – MSKCC
- Lead co-ordinating centre: GOG
- This trial closed due to low recruitment.
- The study results were selected for oral presentation at ASCO 2018 and for the Best of ASCO 2018 meetings, and a manuscript has been accepted for publication in the Journal of Clinical Oncology.



IRCI Relapsed/ Metastatic Anal Cancer Group

InterAAct: A phase II International multicentre randomised advanced anal cancer trial comparing cisplatin plus 5FU vs. carboplatin plus weekly paclitaxel in patients with relapsed or metastatic disease (**IRCI 003**)

- Chief Investigator: Dr Sheela Rao (Royal Marsden Hospital, UK)
- Lead coordinating centre: The Royal Marsden, UK
- The study is the first randomised trial for treatment-naïve metastatic anal cancer patients.
- 92 patients were enrolled across the US, Norway, Australia, and the UK. Enrolment completed in November 2017 and the study is due to be presented at ESMO 2018.
- A further study is planned to build on the InterAAct results, combining the favoured regimen from the initial study with an immunotherapy agent. The study has received approval by the ECOG Steering Committee to move forward for development and will be seeking academic funding shortly.



IRCI Penile Cancer Group

InPACT: International Penile Advanced Cancer Trial (IRCI 004)

- Chief Investigator: Dr Steve Nicholson (Locum Consultant, UK)
- Lead co-ordinating centre: Institute of Cancer Research, UK
- The trial is now recruiting patients at centres in the UK and the US, with centres in Canada due to open shortly. Countries in Central and South America have expressed an interest in participating, along with Australia and India.

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IRCI Rare Skin Cancer Group

General group update:

- This group now covers Merkel Cell carcinoma.
- A trial in Merkel Cell Carcinoma is also being collaboratively developed through the group.



IRCI Rare Melanoma Group

General group update:

- The Rare Melanoma group is planning a full day meeting alongside the 2018 Society for Melanoma Research conference in October, hosted in Manchester UK, at which future trials will be discussed.



IRCI Salivary Gland Cancer Group

EORTC1206-HNCG: A randomised phase II study to evaluate the efficacy and safety of chemotherapy vs. androgen deprivation therapy in patients with recurrent and/or metastatic, androgen receptor expressing, salivary gland cancer (**IRCI 007**)

- Chief Investigator: Dr Lisa Licitra (Istituto Nazionale dei Tumori, Milan, Italy)
- Lead co-ordinating centre: EORTC HQ
- There are currently 62/152 patients recruited across 26 sites in 8 countries.
- The trial is currently open in Austria, Belgium, France, Germany, Hungary, Italy, Greece and the Netherlands. It is anticipated the trial will open later this year in UK and Portugal.



IRCI Small Bowel Adenocarcinoma Group

The BALLAD study: A global study to evaluate the potential benefit of adjuvant chemotherapy for small bowel adenocarcinoma (**IRCI 002**)

- Chief Investigator: Prof Richard Wilson (Belfast, UK)/Prof Jeff Evans (Beatson Cancer Centre, Glasgow, UK)
- Lead coordinating group: Glasgow Clinical Trials Unit, UK
- The study currently has 103/580 patients recruited; 63 patients have been randomised and 40 have been registered.
- The trial is open across the UK and France, and Japan recently opened the study via a parallel protocol. Discussion is currently under way regarding opening in Denmark, the Netherlands, Germany and Portugal.

General group update:

- A multicentre phase II single arm trial with pembrolizumab (MK-3475) in metastatic patients with stage IV disease is currently running in the US; the trial includes translational endpoints.
- There are now 32/40 patients enrolled and full recruitment is expected by fall, with data potentially being available in time for ASCO 2019, or soon thereafter. If the data are encouraging, the trial team intends to discuss a follow-on trial with industry partners.

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IRCI publication list

We have compiled a list of publications from existing working groups as well as other external works referring to IRCI. We hope you will find this a useful reference and this list of publications will be available on the IRCI website in due course. If you know of any additional publications, please let us know.

Essential reading for IRCI trialists

Bogaerts J, et al. Clinical trial designs for rare diseases: Studies developed and discussed by the International Rare Cancers Initiative. *Eur J Cancer* 2015;51:271-81

More about the formation of the International Rare Cancers Initiative

Keat N, et al. The international rare cancers initiative. *J Clin Oncol* 2014;32(suppl):e17504

Keat N, et al. International Rare Cancers Initiative. *Lancet Oncol* 2013;14:109-110

Keat N, et al. International Rare Cancers Initiative (IRCI). *ecancer* 2013;7:10.3332

Publications from IRCI Working Groups: Gynecological sarcoma

Hensley M, et al. Adjuvant gemcitabine plus docetaxel followed by doxorubicin versus observation for uterus-limited, high-grade leiomyosarcoma: A phase III GOG study. *J Clin Oncol* 2018;36(suppl):5505

Publications from IRCI working groups: Penile cancer

Nicholson S, et al. Clinical trial strategy for penis cancer. *BJU Int* 2014;113:852-3

Publications from IRCI Working Groups: Relapsed/metastatic anal cancer

Eng C, et al. Post-treatment surveillance in locally advanced squamous cell carcinoma (SCCA) of the anal canal: A global subspecialist survey. *J Clin Oncol* 2016;34(suppl): abstr 573

Sclafani F, et al. InterAACT: An international multicenter open label randomized phase II advanced anal cancer trial comparing cisplatin (CDDP) plus 5-fluorouracil (5-FU) versus carboplatin (CBDCA) plus weekly paclitaxel (PTX) in patients with inoperable locally recurrent (ILR) or metastatic disease. *J Clin Oncol* 2015;33(suppl): abstr TPS792

Publications from IRCI Working Groups: Rare skin cancer

Khoja L, et al. Meta-analysis of phase II trials in metastatic uveal melanoma (MUM) to determine progression-free (PFS) and overall survival (OS) benchmarks for future phase II trials: An irci-ocular melanoma initiative. *J Clin Oncol* 2016;34(suppl):abstr 9567

Luke J, et al. Biology of advanced uveal melanoma and next steps for clinical therapeutics. *Pigment Cell Melanoma Res* 2015;28:135-47

Publications from IRCI Working Groups: Salivary gland cancer

Locati L, et al. 2018. Hope for salivary gland cancer (SGC): EORTC HNCG/UKCRN 1206 randomized phase II study to evaluate the efficacy and safety of chemotherapy (CT) vs androgen deprivation therapy (ADT) in patients with recurrent and/or metastatic androgen receptor (AR) expressing SGC (NCT01969578). *J Clin Oncol* 2018;36(suppl):abstr TPS6099

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Publications from IRCI Working Groups: Small bowel adenocarcinoma

Pedersen K, et al. Trial in progress: A multicenter phase II study of pembrolizumab in patients with advanced small bowel adenocarcinomas. *J Clin Oncol* 2018;36(suppl):abstrTPS535

Schrock AB, et al. Genomic profiling of small bowel adenocarcinoma: Insights from a comparative analysis with gastric and colorectal cancer and opportunities for targeted therapy. *Ann Oncol* 2016;27(suppl):6130

Evans T, et al. GLOBAL BALLAD: An International Rare Cancers Initiative trial to evaluate the potential benefit of adjuvant chemotherapy for small bowel adenocarcinoma (IRCI 002). *J Clin Oncol* 2016;34(suppl):abstrTPS4154

External works referring to IRCI

Aparicio T, et al. Small Bowel Adenocarcinoma. *Gastroenterol Clin N Am* 2016;45:447-57

Blay J-Y, et al. The value of research collaborations and consortia in rare cancers. *Lancet Oncol* 2016;17:e63

Crook, J. Radiotherapy approaches for locally advanced penile cancer: neoadjuvant and adjuvant. *Curr Opin Urol* 2017;27:62-7

DeSantis C, et al. The Burden of Rare Cancers in the United States. *Ca Center J Clin* 2018;67:261-72

Detterbeck F, Korst R. The International Thymic Malignancy Interest Group Thymic Initiative: A State-of-the-Art Study of Thymic Malignancies. *Semin Thoracic Surg* 2014;26:317-22

Halfdanarson T, et al. Establishing a standard of care for small bowel adenocarcinomas: challenges and lessons learned. *Oncologist* 2012;17:1133

Komatsubara K, Carvajal R. The promise and challenge of rare cancer research. *Lancet Oncol* 2016;17:136-7

Pillai R, et al. Rare Cancers: Challenges and Issues. *Indian J Med Res* 2017;145:17-27

Raghav K, et al. Small bowel adenocarcinomas – existing evidence and evolving paradigms. *Nat Rev Clin Oncol* 2013;10:534-44

Ray-Coquard I, et al. Improving treatment results with reference centres for rare cancers: Where do we stand? *Eur J Cancer* 2017;77:90-8

Roy A, et al. Uncommon Anal Neoplasms. *Surg Oncol Clin N Am* 2017;26:143-61

Schott A, et al. The National Clinical Trials Network: Conducting Successful Clinical Trials of New Therapies for Rare Cancers. *Semin Oncol* 2015;42:731-9

Sclafani F, et al. Systemic Therapies for Advanced Squamous cell Anal Cancer. *Curr Onc Reports* 2018;20:53

Sclafani F, et al. Platinum-Fluoropyrimidine and Paclitaxel-Based Chemotherapy in the Treatment of Advanced Anal Cancer Patients. *Oncologist* 2017;22:402-8

Scott L. Salivary Gland Cancers: The Challenges of Progress in Rare Tumors. *Oncology* 2015;29:781-2

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