Chemotherapy Protocol

GYNAECOLOGICAL CANCERS

RUCAPARIB

Regimen

- Ovarian Cancers – Rucaparib

Indication

- Rucaparib as maintenance treatment in patients with high grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma who have a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have a recent first or subsequent relapse of platinum-sensitive disease and who are now in response following a second or subsequent platinum-based chemotherapy where the:

    - patient has a proven histological diagnosis of predominantly high grade serous or high grade endometrioid or high grade clear cell ovarian, fallopian tube or primary peritoneal carcinoma.
    - patient has had germline and/or somatic (tumour) BRCA testing.
    - patient has a documented deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour or in both.
    - patient has a documented deleterious or suspected deleterious BRCA 1 and/or BRCA 2 mutation.
    - patient had disease which was sensitive to the penultimate line of platinum-based chemotherapy.
    - patient has recently completed a further line of platinum-based chemotherapy and has received a minimum of 4 cycles of platinum-based treatment.
    - patient has responded to the recently completed second or subsequent line platinum-based chemotherapy and has achieved a partial or complete response to treatment according to the following definitions and there is no evidence of progressive disease on the post-treatment scan or a rising CA125 level.

        a) achieved a complete response at the end of the recent 2nd or subsequent line platinum-based chemotherapy i.e. has no measurable or non-measurable disease on the post-chemotherapy scan and the CA125 is normal.
        b) achieved a partial response at the end of the recent 2nd or subsequent line of platinum-based chemotherapy i.e. has had a =30% reduction in measurable or non-measurable disease from the start of to the completion of the 2nd platinum-based chemotherapy or the patient has a complete remission on the post-chemotherapy CT scan but the CA125 has not decreased to within the normal range.

    - the patient is currently less than 8 weeks from the date of the last infusion of the last cycle of the 2nd or subsequent line of platinum-based chemotherapy.

- the patient has not previously received any PARP inhibitor unless Olaparib or niraparib via the CDF has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression;

    a. The patient has never had a PARP inhibitor
    b. The patient has previously received olaparib or niraparib via the CDF and this has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.
    c. The patient previously received rucaparib via an early access scheme and the patient meets all the other criteria listed on blueteq.

- rucaparib will be used as monotherapy.
- patient has a ECOG performance status of either 0 or 1.
- rucaparib will be continued until disease progression or unacceptable toxicity or patient choices to stop treatment.
- there will be a formal medical review as to whether maintenance treatment with rucaparib should continue or not will be scheduled to occur at least by the start of the third cycle of treatment.

- Rucaparib as maintenance treatment in patients with high grade epithelial ovarian, fallopian tube or primary peritoneal carcinoma who do not have a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have a recent first or subsequent relapse of platinum-sensitive disease and who are now in response following a second or subsequent line platinum-based chemotherapy where the:

- patient has a proven histological diagnosis of predominantly high grade serous or high grade endometrioid or high grade clear cell ovarian, fallopian tube or primary peritoneal carcinoma.
- patient has had germline and/or somatic (tumour) BRCA testing.
- patient does not have a document deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour.
- patient had disease which was sensitive to the penultimate line of platinum-based chemotherapy.
- patient has recently completed a further line of platinum-based chemotherapy and has received a minimum of 4 cycles of platinum-based treatment.

  The patient has responded to the recently completed second or subsequent line platinum-based chemotherapy and has achieved a partial or complete response to treatment according to the following definitions and there is no evidence of progressive disease on the post-treatment scan or a rising CA125 level.

    c) achieved a complete response at the end of the recent 2nd or subsequent line platinum-based chemotherapy i.e. has no measurable or non-measurable disease on the post-chemotherapy scan and the CA125 is normal.
    d) achieved a partial response at the end of the recent 2nd or subsequent line of platinum-based chemotherapy i.e. has had a

=30% reduction in measurable or non-measurable disease from the start of to the completion of the 2nd platinum-based chemotherapy or the patient has a complete remission on the post-chemotherapy CT scan but the CA125 has not decreased to within the normal range.

- the patient is currently less than 8 weeks from the date of the last infusion of the last cycle of the 2nd or subsequent line of platinum-based chemotherapy.
- the patient has not previously received any PARP inhibitor unless Olaparib or niraparib via the CDF has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.

    d. The patient has never had a PARP inhibitor
    e. The patient has previously received Olaparib or niraparib via the CDF and this has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.
    f. The patient previously received rucaparib via an early access scheme and the patient meets all the other criteria listed on blueteq.

- rucaparib will be used as monotherapy.
- patient has a ECOG performance status of either 0 or 1.
- rucaparib will be continued until disease progression or unacceptable toxicity or patient choices to stop treatment.
- there will be a formal medical review as to whether maintenance treatment with rucaparib should continue or not will be scheduled to occur at least by the start of the third cycle of treatment.

Toxicity

Drug	Adverse Effect
Rucaparib	Nausea, fatigue, vomiting, anaemia, abdominal pain, taste disturbances, AST/ALT elevations, anorexia, diarrhoea, thrombocytopenia, creatinine elevations, neutropenia, dizziness, dyspepsia, rash, photosensitivity reaction, pyrexia, myelodysplastic syndrome/ acute myeloid leukaemia

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- BRCA testing prior to starting therapy
- FBC, U&Es, creatinine, LFTs every 28 days for the first four cycles (prior to day 1 of the 28 days cycle). There after the patient may be switched to every 56 days for supplies and FBC, U&Es, creatinine and LFTs.
- CA125 where appropriate

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for cancer treatments that if a third dose reduction is necessary treatment should be stopped. Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Recommended dose adjustments

Moderate to severe (grade 3-4) haematological and non-haematological adverse reaction may require dose reduction. The below table provides recommended dose reductions:

Dose reduction	Dose
Starting dose	600mg twice a day
First Dose reduction	500mg twice a day
Second dose reduction	400mg twice a day
Third dose reduction	300mg twice a day

Haematological

Eligible levels to initiate a new cycle;

Test	**Level**
Neutrophils	Greater than or equal to $1.5x10^9$/L
Platelets	Greater than or equal to $75x10^9$/L

If neutrophil's less than $1.5x10^9$/L or platelets less than $75x10^9$/L treatment should be delayed until these levels are achieved and weekly FBCs completed. If the neutrophil or

platelet count has not recovered within 4 weeks the patient should be referred to haematology for further investigations.

During clinical trials 0.5% of patients developed myelodysplastic syndrome (MDS) or Acute Myeloid Leukemia (AML). Patients should be monitored for signs of weakness, fatigue, fever, weight loss, infections, bleeding, bruising, breathlessness and haematological toxicities. If diagnosed with MDS or AML Rucaparib should be permanently discontinued.

Hepatic Impairment

No starting dose adjustment is required for patients with mild or moderate hepatic impairment. Patients with moderate hepatic impairment should be carefully monitored for changes in hepatic function and adverse reactions. There is no data in patients with severe hepatic impairment (ie total bilirubin > 3 times ULN) and rucaparib is not recommended for use in these patients.

Management of treatment-emergent AST/ALT elevations

Liver transaminase elevations can occur early in treatment and are generally transient.

Grade of AST/ALT elevation	Management
Grade 3 without other signs of liver dysfunction	- Monitor LFTs weekly until resolution Grade ≤2 - Continue rucaparib provided bilirubin <ULN and alkaline phosphatase is <3xULN. - Interrupt treatment if AST/ALT levels do not decline within 2 weeks until grade ≤ 2, then resume rucaparib at same or at a reduced dose.
Grade 4	• Interrupt rucaparib until values return to grade ≤ 2, then resume rucaparib with a dose reduction and monitor LFTs weekly for 3 weeks.

Renal Impairment

No starting dose adjustment is required in patients with mild or moderate renal impairment. There is no clinical data in patients with severe renal impairment (CrCl <30ml/min), therefore rucaparib is not recommended in these patients and should only be used where the benefits outweigh the risks. Patients with moderate or severe renal impairment should be monitored carefully for changes in renal function and adverse effects.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Photosensitivity has been observed in patients taking rucaparib. Patients should avoid spending time in direct sunlight as they may burn more easily. Patients should be advised to wear a hat, protective clothing and use sunscreen and lip balm with a sun protective factor of 50 or greater when outside.

Regimen

28 day cycle until disease progression or unacceptable toxicity occurs or the patient chooses to stop treatment (12 cycles will be set in Aria)

Drug	Dose	Days	Administration
Rucaparib	600mg twice a day	Continuous	Oral

Dose Information

- Rucaparib is available as 300mg, 250mg and 200mg film coated tablets.

Administration Information

- The tablets should be swallowed whole and can be taken with or without food.
- The doses should be taken approximately 12 hours apart.
- If a patient vomits after taking rucaparib, the patient shouldn't retake the dose and should take the next scheduled dose.
- If a dose is missed, the next dose should be taken at its scheduled time.
- Rucaparib may have a minor influence on the ability to drive and use machines. Caution when driving or using machines is advised for patients who report fatigue, nausea or dizziness during treatment.

Additional Therapy

- Metoclopramide 10mg three times a day when required oral (this will not be included in the regimen on ARIA but can be added from the support regimens if required)

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to rucaparib.
- It must be made clear to all staff, including those in the community, that rucaparib should only be prescribed under the supervision of an oncologist.
- Rucaparib interacts with other agents. Always check for drug interactions.

References

1. Clovis Oncology UK Ltd (2022). Rubraca 200mg film-coated tablets summary of product characteristics. Available from: www.medicines.org.uk. Accessed 07/07/2022.

REGIMEN SUMMARY

Rucaparib

Cycle 1

1. **Rucaparib 600mg twice a day oral**
   Administration Instructions
   Oral SACT.
   Swallow whole

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2022	None	Alexandra Pritchard Pharmacist	Dr Claire Green Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.