# Clinical Trials Summary for out of hours Important Reference

Lancashire Teaching Hospitals
NHS Foundation Trust

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| **Acronym study title** | **EXELIXIS STELLAR: A Dose-Escalation and Expansion Study of the Safety and Pharmacokinetics of XL092 as Single-Agent and Combination Therapy in Subjects with Inoperable Locally Advanced or Metastatic Solid Tumours** |
| **Study Details** | This study will focus on Prostate/Renal Cancers, randomly assigned to treatment with study drug +/- combination therapy (see below). We are taking part in the dose expansion arm of the study.<br><br>ccRCC (monotherapy)<br>nccRCC (combination therapy)<br>Prostate (combination therapy) |
| **Principal Investigator**<br>**PI**<br>**Sub PIs** | Dr Omi Parikh (Consultant Oncologist, PI) Omi.Parikh@lthtr.nhs.uk<br><br>David Cameron (Research Fellow) David.Cameron@lthtr.nhs.uk |
| **Research Nurse Team** | Karen Jones (Senior Research Nurse) Karen.Jones4@lthtr.nhs.uk<br>Elizabeth Coates (Research Nurse) elizabeth.coates@lthtr.nhs.uk |
| **Drug therapy** | The study drug (XL092) is a new, orally bioavailable, small molecule inhibitor of several Receptor Tyrosine Kinases (RTKs). This treatment aims to disrupt a number of tumour processes including tumour angiogenesis as well as promoting an immune-permissive environment which may enhance response to Immune-Checkpoint-inhibitors (ICIs).<br><br>Atezolizumab is an immunotherapy agent. It is a humanized immunoglobulin that targets programmed death receptor 1 ligand (PD-L1) and inhibits the interactions between LD-L1 and its receptors, which function as inhibitory receptors expressed on T cells. Atelolizumab is already in use in Lung, Urothelial, Breast and Liver Cancers.<br><br>The study drug (XL092) is given via daily oral tablet (fasted two hours before and one hour afterwards). Atezolizumab is given as regular intravenous infusions according to protocol.<br><br>**Adverse Events**<br><br>**Study drug:** Known adverse events associated with single-agent XL092 include hypertension, nausea, diarrhoea, fatigue, deranged liver function, vomiting and headache. Serious adverse events (≥Grade 3, requiring hospitalisation) associated with treatment include AKI, ascites, hypertension, PE, AF, Chest pain, Colitis, Gastritis, headache, hyponatraemia, hypotension, pain and pneumothorax.<br><br>**Atezolizumab:** Treatment with Atezolizumab is generally well-tolerated but can be associated with immune-related adverse events (irAEs) such as hepatitis, pneumonitis, colitis, endocrinopathies, infections and infusion-related reactions<br><br>The most commonly described adverse events have been: Fatigue, Decreased appetite, nausea, urinary tract infection, pyrexia and constipation. Subjects treated with |

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<tr><td></td><td>atezolizumab may also develop Infusion related reactions and Cytokine Release Syndrome as well as immunotherapy AEs such as<br>myocarditis, pneumonitis, hepatitis, colitis, nephritis, endocrinopathies (hypophysitis, thyroid disorders, adrenal insufficiency, Type 1 diabetes), severe cutaneous adverse reactions, skin disorders, ocular events, neurological toxicity (myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome or meningoencephalitis), pancreatitis, myositis.<br><br>AUG 22: The study team have added Pericardial Disorders to the list of possible AEs with Atezolizumab.</td></tr>
<tr><td>In the event that a patient calls this hotline for advice</td><td>Advise patient to seek medical assistance via nearest available healthcare provider depending upon severity of symptoms.<br><br>Advise patient to keep all relevant trial paperwork with them for review by treating clinician Please alert PI/Sub-I/Trial team as soon as possible on LancashireCRF@lthtr.nhs.uk or 01772 522031. Treatment interruptions or dose reductions may be required.<br><br>If needed out of hours contact PI via switchboard</td></tr>
<tr><td>Management</td><td>The study protocol describes management guidelines for common AEs including dose modification criteria. Toxicity is graded using CTCAE v5:<br><br><u>XL092 dose advice based on severity of adverse event</u>
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<tr><td>Toxicity Criteria</td><td>Guidance</td></tr>
<tr><td>Grade 1</td><td>Continue study drug if tolerated, use supportive Care</td></tr>
<tr><td>Grade 2</td><td>Continue study drug if tolerated.<br>If intolerable, hold study drug until toxicity returns to Grade 1</td></tr>
<tr><td>Grade 3</td><td>Hold study drug until toxicity returns to Grade 1 (or baseline). Resume at reduced dose.</td></tr>
<tr><td>Grade 4</td><td>Hold study drug immediately and manage with optimal medical care until toxicity returns to Grade 1</td></tr>
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