Abiraterone

Indication
Castrate resistant metastatic prostate cancer

Newly diagnosed high risk metastatic hormone-sensitive prostate cancer in patients either in whom enzalutamide is contraindicated or who are intolerant of enzalutamide **(interim COVID 19 guidance)**

Regimen details
Abiraterone 1000mg orally daily
Prednisolone 10mg orally daily

Cycle frequency
Continuous treatment, dispense every 1-3 months

Number of cycles
Until disease progression

Administration
Available as 500mg tablets

Abiraterone should be taken at least 2 hours after food and no food should be eaten for at least 1 hour after. Taking food with abiraterone can increase absorption by up to 10 times and therefore can increase toxicity
Steroids should be tapered off slowly when treatment is withdrawn

Pre-medication
n/a

Emetogenicity
n/a

Additional supportive medication
PPI should be prescribed concurrently
Patients should continue on androgen deprivation therapy

Extravasation
n/a

Investigations – pre first cycle

Investigation	Validity period
U+E (including creatinine)	14 days
LFT (including AST)	14 days
LDH	14 days
Testosterone	14 days
PSA	14 days
Blood pressure	baseline

Cautions:
Severe renal impairment
Hepatic impairment (do not use if severe)
Uncontrolled hypertension
History of pituitary or adrenal dysfunction
Contraindication to steroids e.g. poorly controlled diabetes mellitus, active peptic ulceration
Concomitant treatment with strong inducers of CYP3A4

Investigations –pre subsequent cycles

U&Es, LFTs, PSA, LDH
BP and LFTs should be checked every 2 weeks for the first 3 months then every 4 weeks thereafter. (For the first 12 weeks this usually alternates with BP measured by GP alternating with secondary care)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

See under "Dose modifications" below

Dose modifications

For liver toxicity, see table below
For other grade 3 toxicities, suspend treatment. Restart when resolved.

If intolerable side effects within first 12 weeks of treatment and patient is responding, then change to enzalutamide

TOXICITY EVENT	**ACTION**
Grade 1 increases in AST, ALT or bilirubin (e.g. increase in AST or ALT from ULN to 2.5X ULN; increase in total bilirubin from ULN to 1.5X ULN)	The frequency of liver function test monitoring should be increased. No dose reduction is required
Grade 2 increases in AST, ALT or bilirubin (e.g. increase in AST or ALT to >2.5-5X ULN; increase in total bilirubin from >1.5-3X ULN)	The frequency of liver function test monitoring should be increased to ≥ once a week. No dose reduction is required
Grade 3 or 4 increases in AST, ALT or bilirubin (e.g. increase in AST or ALT to >5X ULN; increase in total bilirubin to >3X ULN),	Hold abiraterone and all other concomitant medications that are potentially hepatotoxic. Frequent laboratory evaluations (at least once weekly) should be conducted until the liver function tests return to baseline value or Grade 1
Grade 4 increases in AST, ALT or bilirubin (e.g. increase in AST or ALT to >20x ULN; increase in total bilirubin to >10x ULN)	Discontinue abiraterone immediately. Do not rechallenge. Follow-up until resolution of abnormal liver function tests
RE-CHALLENGE AFTER GRADE 3 INCREASES	**ACTION**
If abiraterone resumption is considered for patients who have experienced Grade 3 increases in AST, ALT, or bilirubin	Resume abiraterone with the first dose level reduction (3 tablets, 750mg) when Grade 3 toxicities resolve to Grade 1 or baseline.
If Grade 3 or higher increases in AST, ALT or bilirubin recur after the first dose reduction	Hold abiraterone and all other concomitant medications that are potentially hepatotoxic. Frequent laboratory evaluations should be conducted (at minimum weekly) until the liver function tests return to baseline value or Grade 1
If abiraterone resumption is considered for patients who have experienced Grade 3 increases in AST, ALT, or bilirubin with the first dose reduction	Resume abiraterone with the second dose level reduction (2 tablets, 500mg) when AST, ALT or bilirubin returns to baseline value or Grade 1

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Cardiac failure
Arrhythmias
Hepatotoxicity
Adrenal insufficiency
Myopathy
Allergic alveolitis

- **Frequently occurring side effects**

Peripheral oedema
Fluid retention
Hypokalaemia
Hypertension
Urinary tract infection
Diarrhoea
Hyperglycaemia

- **Other side effects**

Fractures
Rash

Significant drug interactions

– for full details consult product literature/ reference texts

Medicinal products activated by or metabolised by CYP2D6 (e.g. metoprolol, propranolol, desipramine, venlafaxine, haloperidol, risperidone, propafenone, flecainide, codeine, oxycodone and tramadol): caution is advised when abiraterone acetate is administered with medicinal products activated or metabolised by CYP2D6, particularly with medicinal products that have a narrow therapeutic index. Dose reduction of medicinal products with a narrow therapeutic index that are metabolised by CYP2D6 should be considered.

Codeine, oxycodone and tramadol are metabolised via CYP2D6 to their active metabolites and so abiraterone may have an (as yet unknown) effect on patient's analgesic requirements if treated with these agents.

Strong inhibitors and inducers of CYP3A4 (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, nefazodone, saquinavir, telithromycin, ritonavir, indinavir, nelfinavir, voriconazole) or inducers (e.g., phenytoin, carbamazepine, rifampicin, rifabutin, rifapentine, phenobarbital): avoid or use with caution.

Spironolactone: binds to the androgen receptors and may increase PSA levels. Concomitant use not recommended.

Additional comments

References

Zytiga SPC - https://www.medicines.org.uk/emc/product/2381

South West Clincical Network – chemotherapy protocols http://www.swscn.org.uk/guidance-protocols/cancer-protocols/

THIS PROTOCOL HAS BEEN DIRECTED BY DR BIRTLE, DESIGNATED LEAD CLINICIAN FOR PROSTATE CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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