ISRCTN27617624 https://doi.org/10.1186/ISRCTN27617624

Intravaginal APL202 versus dinoprostone in the induction of labour in nulliparous subjects

Submission date	Recruitment status	[ ] Prospectively registered
15/01/2010	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
15/01/2010	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
19/01/2010	Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
APL202-001

Study information

Scientific Title
A randomised open comparision of intravaginal APL202 (25 or 50 µg) followed by 25 µg after 4 and 8 hours versus 3 mg of dinoprostone as a vaginal tablet followed by 3 mg after 6 hours in the induction of labour in nulliparous subjects

Study objectives
The objective of study APL202-001 was to determine the safety and efficacy of APL202 in the induction of labour of nulliparous subjects compared with the standard agent currently used for cervical ripening.

The trial was previously registered at Pharmaceutical Industry Clinical Trials Database (ABPI /CMR) - https://www.cmrinteract.com/clintrial/default.htm.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Huntingdon Research Ethics Committee approved on the 12th November 2004 (ref: 04/Q0104 /94)

Study design
Randomised open comparative non-inferiority study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Induction of labour - nulliparous subjects only

Interventions
This was a randomised, open, comparative, non-inferiority study. Nulliparous subjects were allocated to one of two groups according to their Bishop score
values and then randomised to one of two treatments. Subjects with Bishop score values of less than or equal to 4 were allocated to Group 1 and randomised to receive one of the two treatments, APL202 or dinoprostone, as follows:
1. APL202 50 µg intravaginally followed by 25 µg intravaginally after 4 and 8 hours
2. Dinoprostone 3 mg intravaginally followed by 3 mg intravaginally after 6 hours

Subjects with Bishop score values less than 9 and greater than or equal to 5 were allocated to Group 2 and randomised to received one of the two treatments, APL202 or dinoprostone, as follows:
1. APL202 25 µg intravaginally followed by 25 µg intravaginally after 4 and 8 hours
2. Dinoprostone 3 mg intravaginally followed by 3 mg intravaginally after 6 hours

The statistical section of the APL202-001 protocol was amended during the course of the study to note that a two-sided analysis would be performed, in line with revised guidelines from the EMEA [Guideline on the choice of the non-inferiority margin, EMEA].

Subjects were randomised equally to each treatment with 506 subjects scheduled to be recruited in conjunction with the same number of subjects in a parallel study APL202-002 (506 were due to be randomised to each treatment). However, a decision was made in 2006 with the

agreement of the ethics and regulatory authorities to pool the data from this study and study APL202-002. This meant that a combined total of 622 subjects, with not more than two-thirds and not less than one-third from either study, were required to be enrolled.

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Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
APL202, dinoprostone

Primary outcome(s)
Number of vaginal deliveries within 24 hours of the start of induction

Key secondary outcome(s))
1. Number of vaginal deliveries within 12 hours of the start of induction
2. Number of caesarean section deliveries
3. Mean induction-delivery interval
4. Distribution of induction-delivery interval
5. Oxytocin augmentation requirement
6. Number of instrument-assisted vaginal deliveries
7. Incidence and mean duration of tachysystole
8. Uterine hyperstimulation with fetal heart rate changes
9. Pyrexia during labour
10. Serious neonatal morbidity or perinatal death
11. Serious maternal morbidity or death

Measured at differing timepoints prior to the discharge of the patients from the hospital after the delivery of the baby.

Completion date
28/02/2007

Eligibility

Key inclusion criteria
1. Subjects, aged 18 years or over, having at least one previous term pregnancy suitable for induction of labour with prostaglandin cervical ripening agents

2. Pregnancy duration of at least 37 weeks
3. Subjects with an unfavourable cervix defined as a Bishop Score of less than 9
4. Signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Subjects requiring insulin to control their diabetes. Subjects with controlled Type II or gestational diabetes that did not require insulin could be included.
2. Subjects with a multiple pregnancy
3. Subjects in whom oxytocic drugs were generally contraindicated or where prolonged contractions of the uterus were considered inappropriate, i.e.:
3.1. History of caesarean section or major uterine surgery
3.2. Cephalopelvic disproportion
3.3. Foetal malpresentation
3.4. Clinical suspicion or definite evidence of pre-existing foetal distress
4. Subjects with an intercurrent vaginal, systemic or ascending infection
5. Subjects with clinical suspicion or definite evidence of placenta praevia or unexplained vaginal bleeding during their pregnancy. Occasional spotting, considered by the Investigator to be of no clinical significance concerning the use of cervical ripening agents and having a reasonable explanation (e.g. cervical ectropion, cervical polyps), was not a reason for exclusion.
6. Subjects with active cardiac, pulmonary, renal or hepatic disease
7. Subjects with abruptio placenta
8. Subjects with ruptured membranes
9. Subjects with a known allergy to prostaglandins or other constituents of the tablets
10. Subjects with any contraindication to vaginal delivery (e.g., active genital herpes)

Date of first enrolment
06/01/2005

Date of final enrolment
28/02/2007

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Alliance Pharmaceuticals Ltd
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Sponsor information

Organisation
Alliance Pharmaceuticals Ltd (UK)

ROR
https://ror.org/001zd1d95

Funder(s)

Funder type
Industry

Funder Name
Alliance Pharmaceuticals Ltd (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2008		Yes	No