



Abraxane for non-small cell lung cancer – first line, in combination with carboplatin

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Target group

- Non-small cell lung cancer (NSCLC): squamous and non-squamous, advanced and/or metastatic (stage IIIb and IV) – first line, in combination with carboplatin.

Technology description

Abraxane is an albumin-stabilised nanoparticle formulation of paclitaxel designed to overcome the insolubility problems associated with conventional paclitaxel formulations. Abraxane utilises albumin binding proteins, such as (gp60)/caveolin-1 (CAV1) and SPARC (secreted protein acidic and rich in cysteine) to achieve high intratumoral paclitaxel accumulation. It eliminates the need for toxic solvents like cremaphor, which are associated with allergic reactions, allowing for the delivery of higher doses and shorter infusion times compared with solvent-based paclitaxel. In clinical trials¹, abraxane is administered by intravenous infusion, at 100mg/m² once a week in combination with carboplatin.

Abraxane is licensed for the treatment of metastatic breast cancer. Recognised adverse effects $\geq 10\%$ include: neutropenia, anaemia, leukopenia, thrombocytopenia, lymphopenia, bone marrow suppression, anorexia, neuropathy, hypoaesthesia, paraesthesia, nausea, diarrhoea, vomiting, constipation, stomatitis, alopecia, rash, arthralgia, myalgia, fatigue, asthenia and pyrexia².

Innovation and/or advantages

If licensed, abraxane may offer an additional treatment option for this patient group.

Developer

Celgene.

Availability, launch or marketing dates, and licensing plans

In phase III clinical trials.

NHS or Government priority area

This topic is relevant to Improving Outcomes: A Strategy for Cancer (2011).

Relevant guidance

- NICE technology appraisal. Erlotinib monotherapy for the maintenance treatment of non-small cell lung cancer. 2011³.
- NICE technology appraisal. Gefitinib for the first line treatment of locally advanced or metastatic non-small cell lung cancer. 2010⁴.
- NICE technology appraisal. Pemetrexed for the maintenance treatment of non-small-cell lung cancer. 2010⁵.
- NICE technology appraisal. Topotecan for the treatment of relapsed small cell lung cancer. 2009⁶.
- NICE technology appraisal. Pemetrexed for the first line treatment of non-small cell lung cancer. 2009⁷.
- NICE technology appraisal. Erlotinib for the treatment of non-small cell lung cancer. 2008⁸.

- NICE technology appraisal. Pemetrexed for the treatment of non-small-cell lung cancer. 2007⁹.
- NICE clinical guideline. Lung cancer: the diagnosis and treatment of lung cancer (update of NICE clinical guideline 24). 2011¹⁰.
- American College of Chest Physicians. Diagnosis and management of lung cancer: ACCP guidelines (2nd Edition). 2007¹¹.
- SIGN. Management of patients with lung cancer. 2005¹².
- European Society for Medical Oncology (ESMO). Metastatic non-small-cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. 2010¹³.
- Cancer Services Collaborative Improvement Partnership. Lung cancer service improvement guide. 2004¹⁴.

Clinical need and burden of disease

In the UK, lung cancer is the most common cause of cancer-related death in men and women. In 2008, there were 34,949 new cases of lung cancer in England and Wales (approximately 48 cases per 100,000 population in the UK)¹⁵ and around 30,254 registered deaths (around 57 deaths per 100,000 population in the UK)¹⁶. In England and Wales, lung cancer has a one-year survival rate of 25% and a five-year survival rate of 7%¹⁷. About 90% of lung cancer mortality among men and 80% among women is attributable to smoking¹¹.

NSCLC accounts for approximately 80% of all lung cancers¹⁷; the main types being squamous cell carcinoma, adenocarcinoma and large cell carcinoma¹⁸. In England and Wales, approximately 75% of newly diagnosed NSCLC patients have advanced (stage III or IV) disease (around 26,200 patients)¹⁹, which has a five-year survival rate of less than 1%¹⁷. An estimated 30% of patients with NSCLC receive first line chemotherapy¹⁷.

Existing comparators and treatments

In advanced NSCLC, treatment aims to relieve symptoms, improve disease control, improve quality of life and increase survival. Treatment options for stage IIIB or IV NSCLC include: radiation therapy, chemotherapy with radiation therapy and chemotherapy alone. Chemotherapy may be recommended for patients provided they have a good performance status^{a,11}.

First line chemotherapy regimens for advanced and/or metastatic NSCLC include^{11,20}:

- A combination of a single third-generation drug (gemcitabine, docetaxel, paclitaxel or vinorelbine) with a platinum drug (carboplatin or cisplatin) or pemetrexed with cisplatin in non-squamous pathology.
- Single agent chemotherapy with a third-generation drug for patients who cannot tolerate a platinum combination.
- Gefitinib for tumours with epidermal growth factor receptor (EGFR) sensitising mutations.
- Bevacizumab plus platinum containing chemotherapy (not recommended by NICE)²¹.
- Maintenance pemetrexed in non-squamous pathology and non progression after first line chemotherapy (not containing pemetrexed).

^a 0 or 1 on the World Health Organisation performance status scale, or a Karnofsky score of 80-100.

Efficacy and safety

Trial	NCT00540514, CA031; abraxane with carboplatin vs paclitaxel and carboplatin; phase III.	NCT00274443, CA028; abraxane with carboplatin; phase II.	NCT00729612, CDR0000602242, OSU-08059, NCCN-AO8; abraxane with carboplatin; phase II.
Sponsor	Abraxis Bioscience, LLC.	Abraxis BioScience, LLC.	National Cancer Institute.
Status	Ongoing.	Complete.	Unknown.
Source of information	Trial registry ¹ , manufacturer.	Trial registry ²² .	Trial registry ²³ .
Location	USA and Canada.	Russia.	USA.
Design	Randomised, active controlled.	Randomised, dose-ranging.	Uncontrolled, single arm.
Participants and schedule	n=1,053 (planned); adults; NSCLC; stage IIIB or IV. Randomised to abraxane, 100mg/m ² weekly plus carboplatin, AUC ^b =6, 3 weekly, or paclitaxel, 200mg/m ² , 3 weekly plus carboplatin, AUC=6, both 3 weekly.	n=250 (planned); adults; NSCLC; stage IIIB or IV. Randomised to abraxane and carboplatin.	n=63 (planned); adults; NSCLC; stage IIIB, IV or recurrent. All patients received abraxane over 30 mins and carboplatin over 1-2 hrs, repeated 3 weekly for up to 6 courses.
Follow-up	Not reported.	Not reported.	Active treatment period 18 wks.
Primary outcomes	Response rate.	AEs; complete response (CR); partial response (PR).	CR; PR.
Secondary outcomes	Progression free survival (PFS); patient survival; disease control rate.	-	Overall survival; PFS.
Key results	For abraxane plus carboplatin and paclitaxel plus carboplatin respectively: overall response rate, %, 33 vs 25 (p=0.005).	-	-
Expected reporting date	Not reported.	Not reported.	Not reported.

Estimated cost and cost impact

The cost of abraxane for NSCLC is not yet known. For breast cancer abraxane costs £246.00 per 100mg vial.

Claimed or potential impact – speculative

Patients

☒ Reduced mortality or increased length of survival

☒ Reduction in associated morbidity or Improved quality of life for patients and/or carers

☐ Quicker, earlier or more accurate diagnosis or identification of disease

☐ Other:

☐ None identified

^b Area Under Curve - carboplatin dosage is calculated from sex, age, weight, height (in obese patients), serum creatinine and target AUC.

Services

- | | | |
|--|---|---|
| <input type="checkbox"/> Increased use | <input type="checkbox"/> Service organisation | <input type="checkbox"/> Staff requirements |
| <input type="checkbox"/> Decreased use | <input type="checkbox"/> Other: | <input checked="" type="checkbox"/> None identified |

Costs

- | | | |
|---|--|---|
| <input checked="" type="checkbox"/> Increased unit cost compared to alternative | <input type="checkbox"/> Increased costs: more patients coming for treatment | <input type="checkbox"/> Increased costs: capital investment needed |
| <input type="checkbox"/> New costs: | <input type="checkbox"/> Savings: | <input type="checkbox"/> Other: |

Other issues

- | | |
|--|---|
| <input type="checkbox"/> Clinical uncertainty or other research question identified: | <input checked="" type="checkbox"/> None identified |
|--|---|

References

- ¹ ClinicalTrials.gov. Patients with advanced non-small cell lung cancer. <http://clinicaltrials.gov/ct2/show/NCT00540514?term=nct00540514&rank=1> Accessed 24 August 2011.
- ² Electronic Medicines Compendium. SPC Abraxane 5mg/ml powder for suspension for infusion. <http://www.medicines.org.uk/EMC/medicine/21384/SPC/Abraxane+5+mg+ml+powder+for+suspension+for+infusion/> Accessed 24 August 2011.
- ³ National Institute for Health and Clinical Excellence. Erlotinib monotherapy for the maintenance treatment of non-small cell lung cancer. Technology appraisal TA227. London: NICE; June 2011.
- ⁴ National Institute for Health and Clinical Excellence. Gefitinib for the first line treatment of locally advanced or metastatic non-small cell lung cancer. Technology appraisal TA192. London: NICE; July 2010.
- ⁵ National Institute for Health and Clinical Excellence. Pemetrexed for the maintenance treatment of non-small-cell lung cancer. Technology appraisal TA190. London: NICE; June 2010.
- ⁶ National Institute for Health and Clinical Excellence. Topotecan for the treatment of relapsed small cell lung cancer. Technology appraisal TA184. London: NICE; November 2009.
- ⁷ National Institute for Health and Clinical Excellence. Pemetrexed for the first line treatment of non-small cell lung cancer. Technology appraisal TA181. London: NICE; September 2009.
- ⁸ National Institute for Health and Clinical Excellence. Erlotinib for the treatment of non-small cell lung cancer. Technology appraisal TA162. London: NICE; November 2008.
- ⁹ National Institute for Health and Clinical Excellence. Pemetrexed for the treatment of non-small cell lung cancer. Technology appraisal TA124. London: NICE; August 2007.
- ¹⁰ National Institute for Health and Clinical Excellence. Lung cancer: the diagnosis and treatment of lung cancer (update of NICE clinical guideline 24). Clinical guideline CG024. London: NICE; April 2011.
- ¹¹ American College of Chest Physicians. Diagnosis and management of lung cancer: ACCP Evidence-based clinical practice guidelines (2nd Edition). Chest 2007; 132(3):744-746.
- ¹² Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with lung cancer. No.80. Edinburgh: SIGN; February 2005.
- ¹³ European Society for Medical Oncology (ESMO). Metastatic non-small-cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2010;21(5):v116-v119.
- ¹⁴ Cancer Services Collaborative Improvement partnership. Lung cancer service improvement guide. October 2004. <http://www.ebc-indevelopment.co.uk/nhs/lung/index.html> Accessed 7 July 2010.
- ¹⁵ Cancer Research UK. Lung cancer - UK incidence statistics. <http://info.cancerresearchuk.org/cancerstats/types/lung/incidence/> Accessed 22 August 2011.
- ¹⁶ Cancer Research UK. Lung cancer – UK mortality statistics. <http://info.cancerresearchuk.org/cancerstats/types/lung/mortality/> Accessed 22 August 2011.
- ¹⁷ National Institute for Health and Clinical Excellence. Final scope for the appraisal of erlotinib monotherapy for the maintenance treatment of advanced or metastatic non-small cell lung cancer. London: NICE; November 2009.
- ¹⁸ Cancer Research UK. Cancer help UK. <http://www.cancerhelp.org.uk/type/lung-cancer/about/types-of-lung-cancer> Accessed 4 August 2011.
- ¹⁹ Liverpool Reviews and Implementation Group, ERG Report – Erlotinib for the treatment of relapsed non-small cell lung cancer. London: NICE; September 2006.
- ²⁰ British Medical Association and Royal Pharmaceutical Company of Great Britain. British National Formulary. BMJ Group and RPS Publishing. London; March 2011.

²¹ National Institute for Health and Clinical Excellence. Bevacizumab for the treatment of non-small-cell lung cancer. Terminated technology appraisal. June 2008.

²² ClinicalTrials.gov. An open label study in patients with advanced NSCLC with ABI-007 (abraxane) in combination with carboplatin. <http://clinicaltrials.gov/ct2/show/NCT00274443?term=nct00274443&rank=1> Accessed 24 August 2011.

²³ ClinicalTrials.gov. Paclitaxel albumin-stabilized nanoparticle formulation and carboplatin in treating patients with stage IIIB, stage IV, or recurrent non-small cell lung cancer. <http://clinicaltrials.gov/ct2/show/NCT00729612?term=nct00729612&rank=1> Accessed 24 August 2011.

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