Clinical Cancer Research in Europe – Plenty of Opportunities to be in the Lead

a report by
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With a population of over 500 million and equal access to excellent healthcare systems in most countries, Europe has enormous potential to lead the world in clinical research programmes in healthcare in general, and in oncology in particular. At the same time, we face some fragmentation and duplication of efforts and witness the effects of the introduction of the European Union (EU)-directives on the conduct of clinical research, which is tripling the cost and doubling the activation time of academic clinical trials.

To overcome these effects we need to firmly believe in our unique opportunities and position of strength, and we must improve interaction between national and European networks to overcome needless competition, avoid duplication and increase speed.

The European Organisation for Research and Treatment of Cancer (EORTC) is increasingly involved in such intergroup trials to secure large quickly accruing trials that will provide answers to crucial questions within reasonable timelines. This will guarantee that the trial results will be important for both defining new standards of care and providing timely building blocks for the next trials.

Science is the driving force behind today's clinical trials, characterised by translational research studies that define mechanisms of action, predict which patients will respond and determine the logical design of further trials. The Trans-BIG/EORTC-MINACT trial on how to effectively use gene profiling in breast cancer is a typical example of the complexity of how to address today's crucial questions that will change the very basis of our clinical treatment decisions.

To successfully conduct such trials one needs the participation of academic institutions with a good research infrastructure. That is why the EORTC is building such a network of core institutes (NOCIs). The EU should intensify programmes to further the formation of such networks to facilitate and solidify scientific and clinical progress.

One may envision various ways to unify our efforts in oncology. The creation of a single European scientific organisation may be a crucial step to help put Europe in the position to meet the challenge to successfully manage the unique opportunities that are within our grasp.

The time to step up to the plate is now. All Europe needs to do is to believe in itself and be aware of the phenomenal annual flow of scientific biomedical publications from Europe. The next step is to make the politicians and the public aware of this. We will only be able to do this if we learn how to communicate and speak with one voice.

New licence for the adjuvant treatment of node-positive, operable breast cancer[1]

Taxotere® has brought significant improvements in survival among patients with metastatic breast cancer – now these benefits extend to the adjuvant setting. New evidence demonstrates that 87% of women treated with adjuvant Taxotere®, in combination with doxorubicin and cyclophosphamide, were alive at 5 years, a 30% relative reduction in risk of death compared to current standard anthracycline-based treatment FAC. Living proof that this Taxotere® based regimen has the potential to save lives.[2]

TAXOTERE® (docetaxel)

Bringing Data To Life

1 - Trade name and presentation:
TAXOTERE, concentrate for solution for infusion, is available in single-dose vials of 0.5 mL or 2 mL, each mL contains 40 mg docetaxel (anhydrous) and 1040 mg polysorbate 80. The diluent contains 13% ethanol in water for injection, and is supplied in vials.

2 - Therapeutic indications:
Breast Cancer: as monotherapy or with capecitabine for locally advanced or metastatic breast cancer after failure of cytotoxic therapy, or with doxorubicin if no previous chemotherapy has been administered for this condition. With trastuzumab for metastatic breast cancer that overexpresses HER2 for which no previous chemotherapy has been administered. With doxorubicin and cyclophosphamide as adjuvant treatment for operable node-positive breast cancer. **Non-Small Cell Lung Cancer (NSCLC):** for locally advanced or metastatic NSCLC after failure of prior chemotherapy and as first line of chemotherapy in combination with cisplatin for unresectable, locally advanced or metastatic NSCLC. **Prostate Cancer:** in combination with prednisone or prednisolone for hormone refractory metastatic prostate cancer. TAXOTERE should be administered under the supervision of a physician qualified in the use of anticancer chemotherapy.

3 - Posology and method of administration:
TAXOTERE is administered intravenously over 1 hour every 3 weeks (3W). **Breast Cancer:** 75 mg/m^2 with doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 every 3 W for 6 cycles and 75mg/m^2 with capecitabine. As monotherapy and with trastuzumab: 100mg/m^2. NSCLC: 75 mg/m^2 as monotherapy after failure of prior platinum-based chemotherapy. 75 mg/m^2 for chemotherapy-naïve patients, followed by cisplatin 75 mg/m^2. **Prostate cancer:** 75 mg/m^2 and Prednisone or prednisolone 5 mg orally twice daily continuously. **Premedication Regimen:** Mandatory with oral corticosteroids for 3 days starting 1 day prior to TAXOTERE administration. For prostate cancer use oral dexamethasone 8 mg, at 12 hours, 3 hours and 1 hour before the TAXOTERE infusion. **Dosage Adjustments During Treatment:** please see full Summary of Product Characteristics (SPC). **Special Populations:** Hepatic Impairment: Patients with bilirubin > ULN should generally not receive TAXOTERE. Also, patients with SGOT and/or SGPT > 1.5 x ULN concomitant with alkaline phosphatase > 2.5 x ULN should receive 75mg/m^2.

4 - Contra-indications:
Hypersensibility to the active substance or to any of the excipients. TAXOTERE should not be used in patients with neutrophil counts of <1500 cells/mm^3. Pregnant or breast-feeding women. Severe liver impairment. For combination consult all the SPCs.

5 - Special warnings and special precautions for use:
Haematology: Neutropenia is the most frequent adverse reaction. Frequent monitoring of blood cell counts should be performed. **Hypersensitivity Reactions:** Patients should be observed closely especially at 1st and 2nd infusion. Hypersensitivity reactions may occur within a few minutes following initiation of the infusion. **Cutaneous:** Localized erythema of the extremities with edema and desquamation were reported. **Fluid Retention:** Patients with severe fluid retention (ascite...) should be monitored closely. **Liver impairment:** See contra-indications, Special population and full SPC. **Nervous system:** Severe peripheral neurotoxicity may require dose reduction. **Cardiac toxicity:** Heart failure may occur when associated with trastuzumab: see full SPC. **Others:** see full SPC.

6 - Drug interactions:
In vitro the metabolism of docetaxel may be modified by compounds metabolized by cytochrome P450 3A.

7 - Pregnancy and lactation:
Women of childbearing potential should be advised to avoid becoming pregnant and breast feeding must be discontinue.

8 - Undesirable effects:
Percentages as **single agent** in patients at 100 mg/m^2 – 75 mg/m^2 respectively: **Haematology:** Severe neutropenia: 76.4 – 54.2, Febrile neutropenia: 11.8 – 8.3, Infection: 20.0 – 10.7, Severe infection: 5.7 – 5.0, Thrombocytopenia: 7.8 – 10.0, Anemia: 90.4 – 93.3, Severe anemia: 8.9 – 10.8, **Hypersensitivity reactions:** 25.9 – 2.5, **Cutaneous reactions:** 56.6 – 13.6, Alopecia: 79.0 – 94.6, Nail changes: 27.9 – 20.2, **Fluid retention:** 64.1 – 24.8, Severe fluid retention: 6.5 – 0.8, **Gastrointestinal:** Stomatitis: 41.8 – 24.8, Diarrhea: 40.6 – 11.6, Nausea: 40.5 – 28.9, Vomiting: 24.5 – 16.5, Constipation: 9.8 – 6.6, Taste perversion: 10.1 – 0, **Nervous system:** Neurosensory: 50.0 – 24.0, Neuromotor: 13.8 – 9.9, **Cardiac disorders:** Cardiac dysrhythmia: 4.1 – 2.5, hypotension: 3.8 – 1.7, 1, hypertension: 2.4 – 0, **Hepato-biliary:** Severe increases of bilirubin: <5 – <2, of alkaline phosphatase: <4 – 0, of AST : <3 – 0, of ALT: <2 – 0, **Others:** Anorexia: 16.8 – 19.0, Severe asthenia: 11.2 – 12.4, Pain: 16.5 – 10.7, Myalgias: 20.0 – 5.8, Dyspnea: 16.1 – 0, Arthralgia: 8.6 – 5.8. Infusion site reaction: 5.6 – <1, Chest pain: 4.5 – 0.

For uncommon, rare and very rare side effects, and for side effects when Taxotere is used in combination with other antineoplasic products: see full Summary of Product Characteristics.

9 - Overdosage:
No known antidote: Therapeutic G-CSF and appropriate symptomatic measures.

10 - Marketing authorisation holder:
Aventis Pharma S.A. 20 avenue Raymond Aron, 92165 ANTONY CEDEX - FRANCE

Abbreviated Prescribing Information based on the EU SPC as of February 2005

References:
1. Taxotere (docetaxel) Summary of Product characteristics sanofi-aventis. **2.** Adjuvant Docetaxel plus Doxorubicin and Cyclophosphamide for Node-Positive Breast Cancer. M. Martin *et al., N Engl J Med* 2005;**352**:2302-13

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