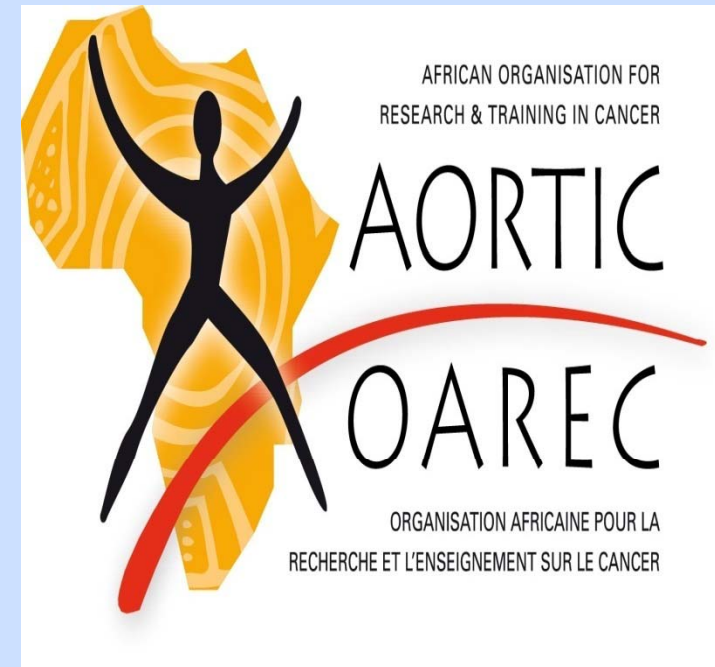


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# Resource sparing in cancer management: Scientific approaches for breast cancer as a model

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By the year 2020, there will be around twenty million new cancer cases, 70% of them in countries with only 5% of total resources for cancer control.

With the increasing costs of the novel drugs and the equipment of radiotherapy, and with the increase of incidence of cancer, we assume that in the next decade, there would be more difficulties of affordability of treatment in Low and Middle Income Countries (LMCs).

The overall and disease-free survival rates, cost effectiveness and cost utility are **not increasing in a measure commensurate** with the expenses of treatment.

Moreover, we assume that the leading pharmaceuticals and radiotherapy equipment companies would face more difficulties in marketing their products in LMCs.

But, to be clear, our concern in this is to increase the affordability of cancer treatment.

Breast Cancer is the most frequent malignancy among females.

Starting with breast cancer systemic therapy BCST as a model , the win-win initiative of ICEDOC's Experts in Cancer without Borders proposed developing –with the main stakeholders- actionable and scientific resource sparing , cost effective and affordable cancer treatment tailored to different regional conditions in the world .

**Two recent articles :**

**Elzawayy AM : Breast Cancer Systemic Therapy: The Need for More Economically Sustainable Scientific Strategies in the World. Breast Care 2008;3:434–438**

(full text is available online in the website of Breast Care, Karger [www.karger.com/brc](http://www.karger.com/brc))

**& Elzawayy A :The "Win-Win" initiative: a global, scientifically based approach to resource sparing treatment for systemic breast cancer therapy .World Journal of Surgical Oncology 2009, 7;44 (Free full text online browse <http://www.wjso.com/content/7/1/44>)**

We extend the scientific review of the current literature to include resource sparing radiotherapy of breast cancer and to update the scientific examples of BCST that we cited previously in the win-win initiative.

The notion of not to compromise the overall outcome is considered.

**For post operative - post mastectomy and post lumpectomy- radiotherapy of breast we cite examples of the published and ongoing scientific ways of resource sparing by:**

**1-Shorten fractionation for post operative radiotherapy ( Hypofractionation):** The example of The UK standardization of breast radiotherapy (START) randomized trial B in which a radiation schedule delivering 40 Gy in 15 fractions offer rates of local-regional relapse and late adverse effects at least as favorable as the standard of 50 Gy in 25 fractions.

**Ref:** The START Trialists' Group: The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet. 2008 March 29; 371(9618): 1098–1107

**2- Less number of radiation fields:** Since systemic adjuvant therapy is given to most patients nowadays, the traditional radiotherapy technique has been modified., it is no longer recommended that patients who have undergone complete or level I/II axillary dissections should receive full axillary radiotherapy since survival is not improved and the risk of lymphoedema is increased. Also, the isolated internal mammary chain failure is rare even when radiotherapy is not given.

**Ref:** Truong PT, Olivotto IA, Whelan TJ, Levine M. Clinical practice guidelines for the care and treatment of breast cancer: 16. Locoregional post-mastectomy radiotherapy. CMAJ 2004; 170 (8): 1261 – 1273.

**For palliative radiotherapy of painful bone metastases** :Shorten fractionation ,up to a single fraction is preferred when examining the cost utility, despite the higher rate of retreatment associated with single-fraction radiotherapy

Ref :van den Hout,W. B.,Y. M. van der Linden, E. Steenland, R. G.Wiggenraad, J. Kievit, H. de Haes, and J. W. Leer .  
Single- Versus Multiple-Fraction Radiotherapy in Patients with Painful Bone Metastases:Cost-Utility Analysis Based on a Randomized Trial.. Journal of the National Cancer Institute 2003; 95 (3): 222–29

**General measures:** That could be done by the local professionals or in consultation with international institutions and regional and/or organizations particularly The International Atomic Energy Agency ( IAEA) and its Program Action for Cancer Therapy (PACT)  
These include:

- General strategic planning of radiotherapy facilities in developing countries.

Ref:Porter A, Aref A, Chodounsky Z, Elzawawy A, Manatrakul N, Ngoma T, Orton C, Van't Hooft E, Sikora K: A global consultation. Clin Oncol strategy for radiotherapy: a WHO (R Coll Radiol) 1999;11: 368–370

## **-The networking of three tier system of teleradiotherapy**

Ref:Datta N , Rajasekar D: Improvement of radiotherapy facilities in developing countries: a three-tier system with a teleradiotherapy network. *Lancet Oncol* 2004; 5: 695–98

- Practical modification of the system of work to treat more numbers of patients**
- Professional customized training for the local staff and maintenance.**

This because the local staff -and not the sophistication in machines- are the back bone of resource sparing and successful cost effective treatment for more number of patients.

By rough estimation of the above cited examples, and without additional expensive resources , it makes like that the facilities of radiotherapy in the world would be- at least -as **doubled!**

## Novel Cancer Drugs:

- The major markets for the pharmaceutical industry are in the USA, Western Europe and Japan.
- Roughly estimated , only **less than 5%** of cancer patients in Low and Middle Income Countries (LMCs), that include the majority of the world's population, could **afford** the **novel** anticancer drugs. This proportion is likely to **decrease** by the year 2020 with **the rise** of expenses of the **novel** drugs .

## For Breast Cancer Systemic Therapy (BCST):

### A) Relatively recent drugs :

- **Evidence based cost effective prescription of drugs:** As the example of the limitation of the use of Trastuzumab in breast cancer to women with non-metastatic disease and known HER2/neu positive status

Yarney J, Vanderpuye V, Clegg Lamptey JN:

Hormone receptor and HER-2 expression in breast cancers among Sub-Saharan African women. Breast J 2008;14:510–511.

**The duration of treatment:** As the example of the shorter course of trastuzumab in The Finher\* trial and others that lead to less total dose of the drug , less total time of hospitalization and less of the subsequent costs of supportive treatment.

\*Joensuu H, Kellokumpu-Lehtinen P L, Bono P, Alanko T, Kataja V, Asola R, Utriainen T, Kokko R, Hemminki A, Tarkkanen M, Turpeenniemi-Hujanen T, Jyrkkio S, Flander M, Helle L, Ingalsuo S, Johansson K, Jaaskelainen AS, Pajunen M, Rauhala M, Kaleva-Kerola J, Salminen T, Leinonen M, Elomaa I, Isola J: Adjuvant docetaxel or vinorelbine with or without trastuzumab for breast cancer. N Engl J Med 2006;354:809–820.

- Low dose, prolonged infusion gemcitabine:  
Hence, the dose for one patient could be  
enough for 4 - 5 patients.

Zwitter M, Kovac V, Smrdel U, Kocijancic I, Segedin B, Vrankar M: Phase I–II trial of low-dose gemcitabine in prolonged infusion and cisplatin for advanced non-small cell lung cancer. *Anticancer Drugs* 2005;16:1129–1134.

## - The International Patient Assistance

**Programs (*like : GIPAP*)** . Lassarat S, Jootar S: Ongoing challenges of a global international patient assistance program. *Ann Oncol* 2006;17(suppl 8):viii43–viii46.

- Pharmacokinetic based studies as in lapatinib therapy, hence the dose for one patient could be enough for five patients!

Ratain MJ, Cohen EE: The value meal: how to save \$1,700 per month or more on lapatinib. *J Clin Oncol* 2007;25:3397–3398.

## **B) Essential and conventional systemic cancer drugs:**

- International measures and initiatives are needed for the assurance of bioequivalence of generics of off-patent drugs.
- Pharmacogenomic studies in order to guide the adjustment of the effective use of some drugs like Tamoxifen.

Brauch H, Schroth W, Eichelbaum M, Schwab M, Harbeck N: Clinical relevance of cyp2d6 genetics for tamoxifen response in breast cancer. Breast Care 2008;3:43–50.

-To test innovative combinations or different schedules of administration of older (and relatively cheaper) previously approved drugs that might lead to improve therapeutic index or more indications .

Examples are :

1-The use of relatively old drug like cisplatin in triple negative breast cancer patients.

Garber JE, Richardson A, Harris LN, Miron A, Silver D, Golshan M: New adjuvant cisplatin (cddp) in 'Triple-negative' Breast cancer (bc). San Antonio Breast Cancer Symposium 2006, abstr 3074.

## 2- The metronomic use of prolonged ,low oral doses of cyclophosphamide and methotrexate as a palliative breast cancer treatment .

Colleoni M, Rocca A, Sandri MT, Zorzino L, Masci ,G, Nole F, Peruzzotti G, Robertson C, Orlando L, Cinieri S, de BF, Viale G, Goldhirsch A: Low dose oral methotrexate and cyclophosphamide in metastatic breast cancer: antitumor activity and correlation with vascular endothelial growth factor levels Ann Oncol 2002;13:73–80.

**3-The more availability of oral forms of chemotherapy that lower the cost of patient transportation, administration and hospitalizations and it may improve the quality of life .**

Elzawayy A. Breast Cancer Systemic Therapy: The Need for More Economically Sustainable Scientific Strategies in the World. Breast Care 2008;3:434–438

**4-In a recent phase II trial, the low dose (10 mg/d) oral estradiol was effective ( around 30% ) as conventional high dose (30 mg/d) ,with less adverse events in postmenopausal women with advanced, ,aromatase inhibitor-resistant, hormone receptor-positive breast cancer.**

Ellis MJ, et al "Lower-dose vs high-dose oral estradiol therapy of hormone receptor-positive, aromatase inhibitor-resistant advanced breast cancer" JAMA 2009; 302(7): 774-80

-The price of Cancer drugs represent only a fraction ( 10-30 % ?) of the cost of breast cancer management.

- Regarding Breast Cancer Systemic therapy in LMCs , there are other factors in -addition to the price of Cancer drugs- that contribute in the cost ,like the needed Hospitalization, the needed transport to the place of treatment , supportive treatment for side effects of cancer drugs and other economic burdens. Hence, we think that reduction of the price of drugs is NOT obligatory the sole solution or approach

As mostly the price of drugs or equipment represent variable fractions from small to moderate parts of the total medical and social cost of cancer chemotherapy and radiotherapy, hence in the win-win initiative we consider the different scientific factors globally.

There are scientific approaches that could lead to resource sparing and eventually for more affordability of breast cancer radiotherapy and systemic therapy in LMCs.

This model could be extended to other cancers in the world. It is recommended to study win-win scenarios for how far could these approaches assure more affordability of such treatment for more millions of patients in the world. and to flourish markets in LMCs for the pharmaceuticals and radiotherapy equipment companies as well.

- The outcome of certain drug are not obligatory the same in all communities ! ( Biology, Pharmacology and pharmcogenomics ....)
- We should consider the quality of life, cost effectiveness or better cost utility , QOLY and DALY for estimation the outcome in different communities in LMCs.
- The notion and estimation of reasonable outcome differs in the same country and not only in between countries.
- There is no one golden model of guidelines for LMCs ( But ,better is the concept of levels of Breast Health Global Initiative BHGI)

**-Pharmaceuticals companies are parts of the - international economy. We like or not, they are main players in development of cancer therapy. We stress on the concept of Win-Win scenarios that all should be transparent & Scientific in this initiative ( No mixing of things or conflicts of interests )**

Since LMCs represent **a small fraction of the pharmaceutical market of expensive drugs**, and with the increasing economic burden of new drugs **,that mostly would shrunk their markets** in those countries in the upcoming years.

Hence, the leading pharmaceuticals companies **wouldn't lose** and hopefully might financially gain more **when they participate** in developing strategies and approaches to face the challenges of affordability of treatment in LMCS. Also, some of proposals could assist facing increasing health bill in richer countries.

**However, to be clear and to avoid confusion , our main concern in our initiative as oncologists is based on the non commercially oriented research scientific work, groups and individuals in LMCs . This what should be more encouraged by both North-South and South –South scientific cooperation.**

**Moreover , surely , scientific cooperation - based on transparency- with industrialists and pharmaceuticals , is welcomed**

**Our main objective –as oncologists and scientists- is toward patients and to lessen the burden of non affordability of treatment on millions of cancer patients.**

While pharmaceuticals and radiotherapy equipment companies, are the best to estimate how they could gain. It is their business and raison d'être.

**Examples of the positive response to the Win-Win initiative coming from the South:**

**The recently launched **ECORN**: The Egyptian Co-operative Oncology Research Network (of SEMCO- EFCR) & the remarkable activities of **ICON** - Indian Co-operative Oncology Network (301 Oncologists from 52 indian cities) who recently expressed their will of collaboration in the Win-Win initiative of ICEDOC**

- **Innovative scientific researches and approaches to cancer control and treatment are needed in LMCs.**
- **We are all living in one planet. There are blames for Oncology as responsible to increase health bill in the USA. Hence, the outcome of such initiatives in LMCs could in return give lights to more cost effective cancer treatment strategies in developed countries!**

## Ongoing and Future directions: ( Patiently but surely progress)

- We are forming of a collaborative task force group and **what Franklin Roosevelt described as "A Brain Trust"**, opened for scientific thoughts and ideas.
- To continue our Data base studies (H.Khaled, A.Elzawayy , A.Badran & SEMCO) and reviews on relevant scientific researches.
- To continue building coalition, cooperation and collaboration links and support
- Published reports .
- Researches projects.

Finally, no leadership role, or claim to invention is being made. There are many key players and stakeholders in the world. Coordination and cooperation are needed

We recommend to study win-win scenarios for how far could these approaches assure more affordability of such treatment for more millions of patients in the world. and to flourish markets in LMCs for the pharmaceuticals and radiotherapy equipment companies as well.

As Prof. David Kerr ,President of ESMO and Prof. Eduardo Cazap ,President of UICC expressed that we know our ways , objectives and we are aware of the difficult challenges” .Hence we should succeed together.

Therefore, we are not like The cheshire cat in the Alice Lewis Carroll’s Masterpiece, who told:

“When you don’t know where you are going, every road will take you there “

**Despite of all challenges, we stress on the necessity of this scientific approach that would be truly “win-win” scenarios in which no one would lose !.**

**Going forward in fruitful cooperation and collaboration ,hands in hands !**

**Thank you all !**

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