Article published online: 2021-07-19

American Society of Clinical Oncology 2014: Updates in breast and gastrointestinal cancers

Shaheenah Dawood

Department of Medical Oncology, Dubai Hospital, Dubai, UAE

Address for correspondence:
Dr. Shaheenah Dawood, Department of Medical Oncology, Dubai Hospital, Dubai Health Authority, P. O. Box 8179, Dubai, UAE.
E-mail: Shaheenah@post.harvard.edu

ABSTRACT

The last two decades have been very exciting in the realm of breast and GI oncology with a plethora of new information that has significantly impacted clinical practice. From the use of anti HER 2 agents in both the adjuvant and metastatic settings of breast cancer to the use of anti EGFR agents in the metastatic setting of colorectal cancer we have seen some significant advances in the treatment of these diseases. This year at ASCO 2014 data were presented that attempted to answer important clinical questions faced by a community oncologist in the clinic. This review focuses on important data presented for both breast and GI cancer.

Key words: *Breast cancer, colon cancer, gastric cancer*

INTRODUCTION

The last two decades have been very exciting in the realm of breast and gastrointestinal oncology. A deeper understanding of the biology of these two malignancies has led to the development of a number of targeted agents that has changed the natural course of these diseases in the metastatic setting and in the case of breast cancer in the adjuvant setting as well. With progress comes a lot of questions that need to be answered when trying to manage your patient in the clinic. This year data presented at American Society of Clinical Oncology (ASCO) 2014 attempted to answer important clinical questions. Is dual human epidermal growth factor receptor-2 (HER-2) blockade important in the adjuvant treatment of breast cancer? Is adjuvant aromatase inhibitor superior to tamoxifen among premenopausal women with breast cancer? Among patients with rat sarcoma wild type metastatic colorectal cancer is bevacizumab or an antiepidermal growth factor (EGFR) more important in the first line setting? Can ramucirumab be used in the first line treatment of metastatic gastric cancer? Here we review interesting abstracts presented at ASCO 2014 that have attempted to answer some of these interesting questions.

Access this article online

Quick Response Code:

Website: www.ijmpo.org

DOI: 10.4103/0971-5851.138997

BREAST CANCER

Strategies to improve adjuvant and neoadjuvant treatment regimens

The role of anthracyclines and taxanes in the treatment of women with early stage breast cancer is well-established. Several trials have investigated whether the addition of agents such as gemcitabine or capecitabine to the standard anthracycline-taxane based adjuvant regimens can further improve prognostic outcome. Moebus *et al.*[1] presented the results of the phase III German Adjuvant Intergroup Node study that randomized approximately 3000 patients with node positive breast cancer (≥4 positive nodes) to either intense dose dense epirubicin, paclitaxel and cyclophosphamide regimen (IDD ETC) or epirubicin and cyclophosphamide followed by paclitaxel and capecitabine (EC-TX). The authors reported that at a median follow up of 74 months 5-year disease free survival was 80% and 82% among those receiving the IDD ETC and EC-TX regimens respectively essentially showing no additional benefit to the addition of capecitabine. Janni *et al.*[2] presented the final results of the phase III SUCCESS: A study that evaluated nearly 4000 patients with high risk breast cancer randomized to receive either fluorouracil (5 FU), epirubicin, and cyclophosphamide (FEC) followed by docetaxel or FEC, followed by docetaxel and gemcitabine. The authors reported a 5-year disease free survival and overall survival of 87% and 93% respectively for both arms of the study thereby concluding that the addition of gemcitabine did not improve prognostic outcome in the cohort study. The results of this study are in line with prior neoadjuvant (NEOTANGO and NSABP 40) and adjuvant (TANGO and NSABP 38) studies that have also failed to show

a benefit of the addition of gemcitabine to a standard anthracycline and taxane based regimen. Data from studies such as these tell us that as of now the chemotherapy backbone of adjuvant regimens remains anthracyclines and taxanes. Future research studies will need to focus not on adding to this standard backbone, but perhaps modifying it according to tumor biology.

American Society of Clinical Oncology 2005 was a momentous occasion for the oncology fraternity in that the results of adjuvant treatment of patients with HER-2 positive breast cancer with trastuzumab were presented at a special session. For the first time in decades the addition of a targeted therapy (trastuzumab) was shown to reduce the risk of death from breast cancer by approximately 50%. Since then several anti-HER-2 agents have been introduced with hope of further improving prognostic outcome among women with HER-2 positive breast cancer. The NEOALLTO and NEOSPHERE studies both showed a significant increase in pathological complete response rates (pCR) when lapatinib or pertuzumab respectively were combined with trastuzumab and chemotherapy. Based on the belief that pCR functions as a surrogate marker of long-term outcome pertuzumab was approved in combination with trastuzumab in the neoadjuvant setting by the Food and Drug Administration in 2013. The question arose as to whether dual blockade actually has an impact on prognostic outcome. Piccart *et al.*[3] presented the results of the phase III randomized ALLTO trial that tried to answer this question. Patients with early stage HER-2 positive breast cancer were randomized to receive adjuvant trastuzumab for 1 year, lapatinib for 1 year, trastuzumab with lapatinib for 1 year or 3 months of tarastuzumab followed by 9 months of lapatinib. Anti-HER-2 therapy could be initiated concurrently with chemotherapy or following completion of all chemotherapy. Three years ago the single agent lapatinib arm of the trial was closed for futility. At median follow-up of 4.5 years no significant difference in the disease free survival and overall survival was observed across the three remaining arms of the study. As such at this time there is no role for the dual blockade in the adjuvant setting. We await the results of the phase III APHINITY trial that is looking at the role of adjuvant dual blockade with a combination of pertuzumab and trastuzumab.

The addition of tamoxifen to the adjuvant treatment of women with hormone receptor positive breast cancer has been shown to reduce the risk of death from breast cancer by 30% among women in the premenopausal age group. The use of luteinizing hormone-releasing hormone agonist has been shown in meta-analysis to have a small additional benefit when used after chemotherapy or in combination with tamoxifen. Adjuvant aromatase inhibitors have been shown among postmenopausal women with hormone receptor positive breast cancer to improve disease free survival compared to tamoxifen. Pagani *et al.*[4] presented the results of the combined results of the SOFT and TEXT trials that randomized premenopausal women with hormone receptor positive breast cancer to either adjuvant tamoxifen and ovarian function suppression or exemestane and ovarian function suppression asking the question of superiority of aromatase inhibitor compared with tamoxifen in this cohort. Women were allowed to receive adjuvant chemotherapy. The authors demonstrated an absolute improvement in disease free survival of 3.8% at 5 years favoring the group of patients receiving exmestane and ovarian function suppression. No significant difference in overall survival was seen although the results were still premature and longer follow-up is required. Based on these results should we be offering the option of an aromatase inhibitor and ovarian function suppression to our premenopausal patients? This option would be associated with increased cost as well as associated toxicity that comes with an aromatase inhibitor and ovarian function suppression. Furthermore, the results of this trial conflicts with the updated results of the ABCSG 12 trial that revealed no difference in disease free survival among between patients receiving tamoxifen and ovarian suppression and those receiving anastrozole and ovarian suppression. Despite this the use of an aromatase inhibitor and ovarian function suppression may be an option to consider among premenopausal women at high risk of relapse. Certainly longer follow-up of this trial is needed. The question of the added benefit of ovarian function suppression compared to no suppression among women receiving tamoxifen will be addressed by the SOFT trial with results expected to be presented later on this year.

Lifestyle and breast cancer

Two interesting oral abstracts were presented that dealt with lifestyle factors that may impact prognostic outcome among women with early breast cancer. Pan *et al.*[5] reported on behalf of the Early Breast Cancer Trialists Collaborative Group pooling individual data from 80,000 patients enrolled in 70 randomized clinical trials dealing with the treatment of early breast cancer. The authors sought to ask the question of whether obesity (defined as a body mass index [BMI] of >30 kg/m^2) had an impact on prognostic outcome among women with early stage breast cancer. The authors reported that compared with women who had normal body weight (defined as BMI 20-25 kg/m^2) obesity was associated with an independent increased risk of breast cancer mortality among premenopausal women with estrogen receptor (ER) positive early stage breast cancer (Relative Risk: 1.34, 95% confidence interval [CI]: 1.22-1.47, 2 $P < 0.00001$) that translated to an absolute 10 year difference in breast cancer mortality of 5%. Furthermore, the investigators noted a clear dose response

relationship with increasing body weight associated with worse prognostic outcome. No significant effect of obesity was noted among women with postmenopausal ER positive disease and those who had ER negative disease. The strengths of this observational study are its large size and availability of individual level data. Limitations of this study include the nonrandomized nature of the study, no information on impact of subsequent weight gain and other life style factors over time, and the fact that it looks at a population of patients enrolled in clinical trials where the rate of obesity was small (23%) and may not be representative of the general population. Nonetheless, the results of the study are striking.

Over the last decade, there has been concern that low levels of Vitamin D is associated with increased risk of breast cancer and poor prognostic outcome in this disease. This stems largely from data derived from observational studies and meta-analysis. At ASCO this year Lohman *et al.*[6] reported on the association of baseline 25 hydroxyvitamin D levels on the relapse free, breast cancer specific and overall survival among patients enrolled in the MA 21 study (a study that randomized over 2000 patients with high risk early stage breast cancer to cytoxan, ellence and 5 FU, AC followed by T or EC followed T). The authors reported no association between pretreatment baseline 25 hydroxyvitamin D levels and the three survival end points of the study. The strengths of this study lie on the prospective nature of the study in a cohort of women that received standardized treatment. The main weakness however include the fact that only blood samples for Vitamin D level assessment was available in only 44% of the patients enrolled in the study, only a small proportion of women enrolled had Vitamin D deficiency (19.3%), Vitamin D levels were only measured at one time point and no data was available on Vitamin D supplementation over the course of time. The authors rightly pointed out that at this time the link between Vitamin D and breast cancer still remain inconclusive and currently there is no data to support the Vitamin D supplementation to improve breast cancer outcomes.

COLORECTAL CANCER

Strategies to improve adjuvant treatment regimens

An important question addressed this year was whether the addition of oxaloplatin to fluoropyramidine based adjuvant therapy decreases risk of disease recurrence among patients with rectal cancer. Hongchao *et al.*[7] presented the results of the phase II ADORE study that randomized 321 patients with curatively resected rectal cancer whose postoperative stage was ypII or III to receive either adjuvant FOLFOX or 5 FU/leucovorin. The authors reported an improvement in 3 year disease free survival from 62.9% to 71.6% favoring the group of patients receiving adjuvant FOLFOX. Rodel *et al.*[8] presented results of a phase III trial where 637 patients with cT3/T4 or CN+ rectal cancer were randomized to receive either preoperative chemoradiation therapy with 5 FU followed by surgery followed by four cycles of adjuvant 5 FU or preoperative chemoradiation therapy with 5 FU and oxaloplatin followed by surgery followed by eight cycles of adjuvant FOLFOX. The authors reported an improvement in 3 year disease free survival from 71.2% to 75.9% ($P = 0.03$) favoring the group receiving oxaloplatin. Both studies indicate a potential role for the use of adjuvant oxaloplatin/5 FU based treatment in patients with rectal cancer at high risk of recurrence.

The presence of microsatellite instability (MSI) in colon cancer is associated with a low recurrence rate postsurgery and resistance to chemotherapy with 5 FU chemotherapy. Tougeron *et al.*[9] presented the results of the multicenter retrospective AGEO study the aim of which was to look at the efficacy of adjuvant chemotherapy with either 5 FU or FOLFOX amongst patients with either high risk stage II or stage III colon cancer. The authors reported a 3 year relapse free survival of 75%, 66% and 84% among patients undergoing surgery alone, receiving adjuvant 5 FU or receiving adjuvant FOLFOX, respectively ($P = 0.02$) essentially indicating that the addition of adjuvant oxaloplatin to a 5 FU back bone chemo sensitivity among patients with MSI colon cancer.

Strategies to improve metastatic treatment regimens

Among patients with *KRAS* wild type metastatic colorectal cancer an important question has been whether to start with either bevacizumab or an anti-EGFR agent with chemotherapy as first treatment in this cohort. Last year we saw the results of the FIRE 3 study presented at ASCO 2013, which indicated that among patients with *KRAS* wild type metastatic colorectal cancer a significantly superior overall survival was observed favoring patients receiving cetuximab plus FOLFIRI compared to those receiving bevacizumab plus FOLFORI. This year Venook *et al.*[10] reported on the CALGB/SWOG 80405 study that is the largest phase III trial among patients with *KRAS* wild type metastatic colorectal cancer that compared head to head first line treatment with cetuximab plus chemotherapy to bevacizumab plus chemotherapy. The study was designed as a superiority study with the primary end point being overall survival. The majority of patients received FOLFOX as the chemotherapy backbone. The study did not meet its primary end point with no difference in overall survival or progression free survival observed between the two arms of the study.

At ASCO 2013 a number of important abstracts were presented looking at the role of maintenance treatment

following induction chemotherapy among patients with metastatic colorectal cancer. This year Arnold *et al.*[11] presented the results of the phase III noninferiority AIO KRK 0207 trial that looked at the impact of observation, fluoropyrimidine plus bevacizumab or bevacizumab alone following a 24 week induction regimen of fluoropyramidine/oxaloplatin/bevacizumab. At a median follow-up of 27 months the authors reported a time to failure strategy of 3.6 months, 6.2 months and 4.6 months among patient receiving no treatment, fluoropyrimidine plus bevacizumab or bevacizumab alone, respectively ($P < 0.001$). The results of this study essentially confirmed the results of the CAIRO-3 and SAKK studies presented at ASCO 2013.

Delving into the biology of colorectal cancer

A number of interesting abstracts were presented this year that gave us deeper insight into the biology of colorectal cancer. It has long been reported that receptor status of breast tumors can change over time with an almost 30% discrepancy reported across a number of studies between the primary and metastatic sites. In colon cancer a high degree of concordance of *KRAS* has been shown among primary and metastatic tumors. Kopetz *et al.*[12] reported on the discordance in mutation and copy number of a number of mutated genes between primary and metastatic colorectal tumors. One hundred and seven pairs of primary and metastatic tumors were sequenced on a 46 or 50 gene hotspot AmpliSeq panel (Ion Torrent) panel and targeted re sequencing of a panel of 202 genes by HiSeq 2000 (ILLumina) was performed on 17 patients. 46 high level amplifications were found in 28 genes in 11 of the 17 pairs that were subjected to targeted sequencing, which were discordant between the 202 gene panel and the 46/50 gene panel. Examples of clinically relevant discordant genes included *HER2, NOTCH1, FLT3*, and *AURKA*. The authors reported 6.8-fold higher odds of discordance between primary and metastatic site for the *PIK3CA,* while a similar concordance to *KRAS* (89% concordance) was demonstrated for *APC, TP53, NRAS,* and *BRAF*. Interestingly the authors further reported that intervening chemotherapy was associated with a 3.5-fold higher odds of discordance between primary and metastatic tumors across all genes compared to those who had not received chemotherapy.

Several molecular subtypes of colorectal cancer have been proposed. Dienstmann *et al.*[13] reported on behalf of the colorectal cancer subtyping consortium that conducted a formal comparison across different classifiers to identify a consensus among the different subtyping systems through large scale data sharing and meta-analysis. The consortium analyzed more than 30 patient cohorts with gene expression data and identified four colorectal cancer subtypes (CMS1-4) with each subtype enriched for key clinical, pathway and molecular traits. The proposed classification may have significant implications on future research and clinical practice.

NONCOLORECTAL CANCER

2014 has been a significant year for gastric cancer with ramuciurmab, a human immunoglobulin G1 vascular endothelial growth factor-receptor-2 targeted antibody, found to be efficacious both as a single agent and in combination with paclitaxel among patients with metastatic gastric adenocarcinoma following progression of disease on previous platinum and fluropyrimadine based treatment. At ASCO 2014 two interesting abstracts were presented looking at this compound. Hironaka and colleagues[14] reported on the efficacy analysis among Japanese and Western patients in the RAINBOW trial that is a global phase III trial of patients with metastatic gastroesophageal junction and gastric adenocarcinoma randomized to ramucirumab plus paclitaxel or placebo plus paclitaxel following disease progression. The authors reported a significant improvement in progression free survival, objective response rate and 6 month overall survival favoring the group receiving ramucirumab among both Japanese and Western patients. Interestingly the authors further reported no difference in overall survival in the Japanese cohort but significant improvement in overall survival in the Western cohort with the addition of ramucirumab. One possible reason for the lack of overall survival benefit in the Japanese cohort could be the generally the better overall survival observed among the Japanese cohort compared to the Western cohort resulting in an ability to deliver subsequent lines of therapy that would obscure any overall survival benefit observed from the progression free survival benefit.

Following the remarkable success of ramucirumab in the second line and beyond metastatic setting the next step was to evaluate its efficacy in the first line setting. Yoon *et al.*[15] reported on a phase II double blind, multicenter trial that randomized 168 patients with untreated metastatic or local advanced gastric or esophageal adenocarcionoma to either FOLFOX plus ramucirumab or FOLFOX plus placebo. Interestingly there was no significant difference in the progression free survival or overall survival between the two groups. Several questions have been raised by the results of this study. First is the type of chemotherapy backbone that ramucirumab is combined with important? Paclitaxel may be a better option compared to FOLFOX. Second, an exploratory analysis presented by the authors revealed a lack of progression free survival benefit with the addition of ramucirumab among patients with metastatic

esophageal cancers hazard ratio (HR: 1.10, 95% CI: 0.61-1.97, $P = 0.746$), while a significant improvement was observed among those with gastroesophageal junction tumor or gastric tumor (HR: 0.53, 95% 0.29-0.97, $P = 0.036$) raising the question of whether trials with the agent should focus only on patients with gastroesophageal junction tumor or gastric tumors.

Bruix *et al*.[16] presented the results of the STORM a phase III randomized, placebo controlled trial looking at the efficacy of adjuvant sorafenib among patients after resection or ablation among patients with hepatocellular carcinoma. The authors reported no difference in recurrence free survival, time to recurrence or overall survival. This is in keeping with the lack of benefit seen for targeted agents used to date that have been investigated in the adjuvant setting.

REFERENCES

1. Moebus VJ, Von Minckwitz G, Jackisch C, Lueck HJ, Schneeweiss A, Tesch H, *et al*. German Adjuvant Intergroup Node Positive (GAIN) study: A phase III trial to compare IDD-ETC versus EC-TX in patients with node-positive primary breast cancer – Final efficacy analysis. J Clin Oncol 2014;32:5s. [Suppl; abst].
2. Janni W, Schneeweiss A, Haeberle L, Fasching PA, Sommer HL, Rezai M, *et al*. Adjuvant gemcitabine for high-risk breast cancer (BC) patients: Final survival results of the randomized phase III SUCCESS - A study. J Clin Oncol 2014;32:5s. [Suppl; abstr 1010].
3. Piccart-Gebhart MJ, Holmes AP, Baselga J, De Azambuja E, Dueck AC, Viale G, *et al*. First results from the phase III ALTTO trial (BIG 2–06; NCCTG [Alliance] N063D) comparing one year of anti-HER2 therapy with lapatinib alone (L), trastuzumab alone (T), their sequence (T→L), or their combination (T + L) in the adjuvant treatment of HER2-positive early breast cancer (EBC). J Clin Oncol 2014;32:5s. [Suppl; abstr LBA4].
4. Pagani O, Regan MM, Walley B, Fleming GF, Colleoni M, Lang I, *et al*. Randomized comparison of adjuvant aromatase inhibitor (AI) exemestane (E) plus ovarian function suppression (OFS) vs tamoxifen (T) plus OFS in premenopausal women with hormone receptor-positive (HR+) early breast cancer (BC): Joint analysis of IBCSG TEXT and SOFT trials. J Clin Oncol 2014;32:5s. [Suppl; abstr LBA1].
5. Pan H, Gray RG. On Behalf of the Early Breast Cancer Trialists' Collaborative Group; Effect of obesity in premenopausal ER + early breast cancer: EBCTCG data on 80,000 patients in 70 trials. J Clin Oncol 2014;32:5s. [Suppl; abstr 503].
6. Lohmann AE, Chapman JA, Margot J, *et al.* Prognostic associations of 25OH vitamin D in NCIC CTG MA.21, a phase III adjuvant RCT of three chemotherapy regimens (EC/T, CEF, AC/T) in high-risk breast cancer (BC). J Clin Oncol 2014;32:5s. [Suppl; abstr 504].
7. Hong YS, Nam BH, Kim KP, Lee JL, Park JO, Park YS, *et al.* Adjuvant chemotherapy with oxaliplatin/5-fluorouracil/leucovorin (FOLFOX) versus 5-fluorouracil/leucovorin (FL) for rectal cancer patients whose postoperative yp stage 2 or 3 after preoperative chemoradiotherapy: Updated results of 3-year disease-free survival from a randomized phase II study (The ADORE). J Clin Oncol 2014;32:5s. [Suppl; abstr 3502].
8. Rodel C, Liersch T, Fietkau R, Hohenberger W, Graeven U, Hothorn T, *et al*. Preoperative chemoradiotherapy and postoperative chemotherapy with 5-fluorouracil and oxaliplatin versus 5-fluorouracil alone in locally advanced rectal cancer: Results of the German CAO/ARO/AIO-04 randomized phase III trial. J Clin Oncol 2014;32:5s. [Suppl; abstr 3500].
9. Tougeron D, Sickersen G, Lecomte T, Mouillet G, Trouilloud I, Coriat R, *et al.* Impact of adjuvant chemotherapy with 5-FU or FOLFOX in colon cancers with microsatellite instability: An AGEO multicenter study. J Clin Oncol 2014;32:5s. [suppl; abstr 3508].
10. Venook AP, Niedzwiecki D, Lenz HJ, Innocenti F, Mahoney MR, O'Neil BH, *et al*. Cancer and Leukemia Group B (Alliance), SWOG, and ECOG; CALGB/SWOG 80405: Phase III trial of irinotecan/5-FU/leucovorin (FOLFIRI) or oxaliplatin/5-FU/leucovorin (mFOLFOX6) with bevacizumab (BV) or cetuximab (CET) for patients (pts) with KRAS wild-type (wt) untreated metastatic adenocarcinoma of the colon or rectum (MCRC). J Clin Oncol 2014;32:5s. [Suppl; abstr LBA3].
11. Arnold D, Graeven U, Lerchenmuller CA, Killing B, Depenbusch R, Steffens CC, *et al.* Maintenance strategy with fluoropyrimidines (FP) plus Bevacizumab (Bev), Bev alone, or no treatment, following a standard combination of FP, oxaliplatin (Ox), and Bev as first-line treatment for patients with metastatic colorectal cancer (mCRC): A phase III non-inferiority trial (AIO KRK 0207). J Clin Oncol 2014;32:5s. [Suppl; abstr 3503^].
12. Kopetz S, Overman MJ, Chen K, Lucio-Eterovic AK, Kee BK, Fogelman DR, *et al*. Mutation and copy number discordance in primary versus metastatic colorectal cancer (mCRC). J Clin Oncol 2014;32:5s. [Suppl; abstr 3509].
13. Dienstmann R, Guinney J, Delorenzi M, Reynies AD, Roepman P, Sadanandam A, *et al.* Colorectal Cancer Subtyping Consortium; Colorectal Cancer Subtyping Consortium (CRCSC) identification of a consensus of molecular subtypes. J Clin Oncol 2014;32:5s. [Suppl; abstr 3511].
14. Hironaka S, Shimada Y, Sugimoto N, Komatsu Y, Nishina T, Yamaguchi K, *et al.* RAINBOW: A global, phase III, randomized, double-blind study of ramucirumab (RAM) plus paclitaxel (PTX) versus placebo (PL) plus PTX in the treatment of metastatic gastroesophageal junction and gastric adenocarcinoma (mGC) following disease progression on first-line platinum-and fluoropyrimidine-containing combination therapy-Efficacy analysis in Japanese and Western patients. J Clin Oncol 2014;32:5s. [Suppl; abstr 4005].
15. Yoon HH, Bendell JC, Braiteh FS, Firdaus I, Philip AP, Cohn AL, *et al.* Ramucirumab (RAM) plus FOLFOX as front-line therapy (Rx) for advanced gastric or esophageal adenocarcinoma (GE-AC): Randomized, double-blind, multicenter phase 2 trial. J Clin Oncol 2014;32:5s. [Suppl; abstr 4004].
16. Bruix J, Takayama T, Mazzaferro V, Chau GY, Yang J, Kudo M, *et al.* STORM: A phase III randomized, double-blind, placebo-controlled trial of adjuvant sorafenib after resection or ablation to prevent recurrence of hepatocellular carcinoma (HCC). J Clin Oncol 2014;32:5s. [Suppl; abstr 4006].

How to cite this article: Dawood S. American Society of Clinical Oncology 2014: Updates in breast and gastrointestinal cancers. Indian J Med Paediatr Oncol 2014;35:176-80.
Source of Support: Nil. **Conflict of Interest:** None declared.