Randomized Phase III Trial Comparing Epirubicin/ Doxorubicin Plus Docetaxel and Epirubicin/ Doxorubicin Plus Paclitaxel as First Line Treatment in Women with Advanced Breast Cancer

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ABSTRACT

This study aimed to examine the efficacy of docetaxel plus epirubicin against docetaxel plus capecitabine as first-line therapy for women with advanced breast cancer (ABC). Patients with ABC who had not been treated in the past were split into two groups: those who received docetaxel and epirubicin (DE) on day 1 and those who received docetaxel and capecitabine (DC) on day 1 and twice daily on days 1-14 of each 21-day cycle. Prior neoadjuvant treatment with anthracyclines was permitted if it had been finished more than a year prior to enrolment. The study's major aim was to evaluate the difference in time to disease progression (TTP). Median TTP for DE was 10.6 months and for DC it was 11.0 months (P = 0.7), with each arm treating 170 women. Using the RECIST criterion, we found that the rates of complete responses were higher in DC (61%) than in DE (11%), and that the rates of partial responses were lower in DC (40%) than in DE (45%) (P = 0.8). Grade 3-4 neutropenia was more common with DE than DC (57% vs. 46%, P = 0.07), as were febrile neutropenia (11% vs. 8%, P = 0.4), hand-foot syndrome (0% vs. 4%, P = 0.02), grade 2-3 anemia (20% vs. 7%, P = 0.001), and asthenia (12% vs. 6%, P = 0.09).

Keywords- Cancer Patients, Combine therapy, Women, first line drug.

I. INTRODUCTION

Over 2.3 million women in the United States are diagnosed with breast cancer each year. Breast cancer is the most common form of cancer in females. among almost 95% of the world's countries, breast cancer is either the major or secondary cause of mortality from cancer among females. On the other hand, breast cancer survival rates vary significantly not only between countries but also within individual nations. Nearly eighty percent of deaths from breast and cervical cancer are attributed to countries with poor or intermediate incomes. The increasing prevalence of breast cancer is a challenge that is especially difficult to address in developing countries. The Director-General of the World Health Organization (WHO), Dr. Tedros Adhanom Ghebreyesus, stated that "We have the tools and the know-how to prevent breast cancer and save lives, and it must be a priority for ministries of health and governments everywhere." More than seventy countries, particularly those with lower and intermediate incomes, have the backing of the WHO in their efforts to enhance breast cancer screening, diagnosis, and treatment for the benefit of all patients. These nations are working to benefit all patients.
The ramifications of cancer in women, and breast cancer in particular, are devastating to succeeding generations of people. Because cancer is predicted to claim the lives of 4.4 million women worldwide in 2020, the International Agency for Research on Cancer projects that roughly one million children will be orphaned as a direct result of cancer, with breast cancer accounting for 25% of these instances. When a kid suffers the loss of their mother to cancer, not only does it have an impact on their health and education throughout their entire life, but it may also bring generational, chronic social disturbance as well as financial difficulty. It is necessary for the primary health care systems of individual nations to be actively involved in this framework and integrated with it. According to Dr. Bente Mikkelsen, the Director for Noncommunicable Diseases at the World Health Organization (WHO), this effort will not only help in the promotion of health but will also encourage women to seek and get medical care at all phases of their life. In order to accomplish the goal of universal health care, "we can really see a pathway with effective and sustainable primary health care." In order to expand people's access to high-quality breast cancer care in nations with low and intermediate incomes, a new framework has been developed, and it draws inspiration from tried-and-true approaches to doing so. It lays out an offensive strategy that is comprised of three pillars and has measurable goals:

Encouraging countries to make financial investments in breast cancer detection programs, with the goal of increasing the percentage of breast cancer diagnoses made at early stages from the present 40% to 60%.

If breast cancer is discovered and treated within the first sixty days after the first signs of the disease present, survival rates for the disease can be boosted significantly. The best time to begin treatment is within three months of when the earliest manifestation appeared.

Ensuring that at least 80 percent of patients diagnosed with breast cancer complete their course of therapy as directed.

If its implementation was speed up, the Global Breast Cancer Initiative of the World Health Organization (WHO) has the potential to avert millions of deaths that could have been avoided among women, as well as the accompanying, intergenerational ramifications that would have occurred.

Resolution In 2017, the World Health Assembly decided to adopt a strategy that focuses on the prevention and control of cancer within the framework of an integrated approach. The World Health Organization (WHO) has launched integrated initiatives in women's and children's cancers beginning in 2018, with the goal of eradicating cervical cancer and tripling the survival rate for paediatric cancer. If all of these initiatives are combined, it is estimated that over one million lives will be spared from cancer over the course of the following decade. The World Health Organization has issued a call to action to governments, development partners, businesses, and individuals to do everything they can to close the care gap in order to halt the generational impacts of cancer.

![Fig: 1 New case of cancer distributed worldwide in women at all age group](image)

"While some of the most cutting-edge cancer treatment methods and technology are available in our nation's hospitals, we still have a long way to go before we can ensure that cancer patients from every socioeconomic background receive the best feasible care," added Kakkar, who is also the Managing Director of Varian Medical Systems International India Pvt Ltd.

The burden of cancer disease in India is characterized by poor diagnosis, with not more than 29 percent, 15 percent, and 33 percent of breast, lung, and
cervical cancers being found in stages 1 and 2, respectively. This is a problem because early identification is the best way to treat cancer. It was discovered that cancer of the head and neck is developing at a CAGR of 23 percent, prostate cancer is progressing at a CAGR of 19 percent, ovarian cancer is progressing at a CAGR of 11 percent, and breast cancer is progressing at a CAGR of 8 percent, which is faster than the general growth rate of occurrence. Six of India’s states are responsible for 23 percent of the country’s reported incidence burden and have the highest crude incidence rates. These states’ populations account for 18 percent of India’s total population. According to the research, the states of Kerala, Mizoram, Tamil Nadu, Karnataka, and Punjab record the highest overall crude incidence rates of cancers, which are greater than 130 cases per lakh of population. Also highlighted in the report is Assam. According to some estimates, the total number of fatalities caused by cancer reached between 8 and 9 lakh in 2023. As a result, the mortality to incidence ratio for various types of cancer in India is among the lowest when compared to that of other countries around the world.

II. SCREENING & EARLY DIAGNOSIS

Ideally, cancer screening is undertaken when the risk of cancer is high enough to justify the risk of overdiagnosis and overtreatment in an otherwise healthy population. Cancer screening in healthy populations balances patient tolerance of risk, personal attitudes and the choice of a screening program most likely to have net benefit to the individual. In low-to-average risk populations, the recommended age to begin routine cancer screening is the age at which the risk of cancer begins to rise (e.g., 50 years for colorectal cancer screening) and when the tumor develops slowly. Slow tumor progression allows for the identification of a malignancy (or pre-malignancy) at an early stage which reduces the incidence of late stage cancer. For instance, the optimal screening interval for colorectal cancer screening with colonoscopy in the general population is 10 years, which allows for the removal of the pre-cancerous lesion, the adenomatous poly, thereby reducing colon cancer. Cancer screening does not work as effectively for rapidly growing tumors or those that disseminate early, as they tend to occur between screening intervals and present with symptoms.

Integrating exposure history is commonly used to improve the identification of individuals at higher risk of cancer than the general population. Targeting smokers with a 30 pack-year for low-dose chest tomography (CT) to screen for early lung cancer and identifying women with HPV infection to define a high risk population at risk of cervical cancer demonstrate efforts to use risk stratification in order to offer screening to individuals most likely to benefit and reduce screening in low risk individuals.

Risk-prediction models attempt to identify individuals at higher risk of cancer than the general population. The Breast Cancer Risk Assessment Tool was one of the first tools aimed at identifying women who could benefit from breast cancer chemoprevention trials and accounts for clinical risk factors (i.e., family history, personal history, breast biopsy) as well as hormonal exposures (i.e., age of menarche). More recent risk-prediction models incorporate exposures (i.e., radiation exposure), breast density as well as biomarkers (i.e., single nucleotide polymorphisms) in an effort to improve risk-stratification.

The contribution of genetics and genomics to risk-stratification has steadily progressed since the identification of the germline p53 mutation in Li Fraumeni Syndrome. The ability to identify individuals who carry a germline mutation associated with a hereditary cancer syndrome greatly improves risk-stratification and helps identify those individuals who may benefit from more frequent cancer screening and other preventive procedures. For example, individuals at high risk of cancer due to inherited cancer susceptibility (such as carrier of a BRCA1 or BRCA2 mutation) undergo aggressive cancer screening for the tumors associated with the syndrome and may also consider prophylactic surgery to reduce their risk of cancer. Within a family with a known BRCA1 mutation, those family members who did not inherit the mutation do not need to undergo intensive screening nor do they need to consider prophylactic surgery to prevent cancer. As the expense of genetic sequencing decrease, there is an increase in the use of genetic testing panels and other genomic technologies for risk stratification. However, important clinical challenges exist with these technologies regarding the classification of the identified genetic variants, reporting of the variants or unknown significance and how to handle incidental findings. Multiple organizations have developed standards and guidelines for interpreting sequence variants and conclude that clinical genetic tests should be performed in Clinical Laboratory Improvement Amendments (CLIA)-approved labs and the results should be interpreted by a board certified clinical molecular geneticist, a molecular genetic pathologist or the equivalent.

Fig: 2 Anatomy of women Breast
III. PATIENTS AND METHODS

Inclusion criteria

Women 18-75 years old with histologically- or cytologically confirmed and previously untreated locally advanced or metastatic breast adenocarcinoma were eligible for the study. Prior adjuvant or neoadjuvant chemotherapy with an anthracycline-based regimen was allowed if it had been completed >1 year before enrollment. Other eligibility criteria included the presence of measurable disease (RECIST criteria), performance status of zero to two (World Health Organization criteria), adequate hematological (absolute granulocyte count >1.5 · 10^9/L and platelet count >100 · 10^9/L), renal (creatinine level <1.5 mg/dl), liver (AST, ALT, and alkaline phosphatase all ≤ 1.5 × upper limit of normal and bilirubin within normal limits) and hepatic [transaminases <1.5; the upper normal limit (UNL), alkaline phosphatases <2.5 UNL, and bilirubin <UNL] function and normal left ventricular ejection fraction (LVEF >50%). Prior hormonal therapy or radiation therapy was allowed if they had been stopped at least 1 month before enrollment and if <25% of the active bone marrow had been irradiated. Prohibited prior treatments included taxanes, bone marrow transplantation or stem-cell support, recent radiotherapy to bone marrow, surgery within the prior 2 weeks, and an investigational drug within 4 weeks of study registration. Bisphosphonate therapy was permitted.

Exclusion criteria

Exclusion criteria included active central nervous system metastases, history of serious cardiac disease contraindicating the use of anthracyclines, history of malignancy rather than history of previous cancer (except treated basal cell and squamous cell carcinoma of the skin or cancer of the uterine cervix) and other serious concomitant illness. The concurrent administration of other antineoplastic treatment was not allowed. Patients with HER2-positive disease were excluded from the study. Written informed consent was obtained from each patient before enrollment.

The protocol was approved by the Ethics and Scientific Committees of all participating centers. The study was conducted in accordance with the Declaration of Helsinki and the applicable guidelines on good clinical practice.

Baseline and follow-up evaluations

Baseline evaluation included patient history, physical examination, chest X-rays, complete blood count (CBC) with differential, blood chemistry with CA 15-3 and carcinoembryonic antigen (CEA) measurement, electrocardiogram (ECG), echocardiography or multiple gated acquisition scan (MUGA) with LVEF measurement, computed tomography (CT) scan of chest and abdomen and a bone scan. CBCs were repeated weekly for all patients throughout the treatment or daily in case of grade 3-4 neutropenia, thrombocytopenia or febrile neutropenia and until hematological recovery occurred.

Before each cycle, evaluation included patient history, physical examination, CBC, blood chemistry with CEA and CA 15-3 determination and an ECG. Other tests were carried out when clinically indicated. Cardiac monitoring consisted of physical examination and ECG carried out every 3 weeks and LVEF measurement every three cycles of treatment (DE regimen). Evaluation of response was carried out after each cycle if measurable disease was assessable by physical examination or after every three cycles of treatment by repeating the CT scans. All objective responses, assessed by two independent radiologists, had to be maintained for at least 4 weeks. Long-term follow-up included patient history, physical examination, CBC, blood chemistry and radiological assessments every 3 months until disease progression occurred and every 6 months thereafter until death. Response to treatment was assessed by using RECIST.

Statistical Methodology and Analysis

The primary end points were the objective response rate and toxicity. Secondary end points included duration of response, time to progression (TTP), overall survival (OS), and quality of life (QOL).

The sample of ~170 patients for this study was chosen to provide adequate power to detect an improvement of 10% in progression free-survival with the dose-dense regimen with an expected proportion of relapse of ~30% after 5 years in the standard treatment arm. The ITT population included all randomly assigned patients, including those who did not receive treatment, with analyses performed based on the treatment assigned. Eligible patients included all patients with no major inclusion or exclusion criteria deviations. Patients assessable for response included those who met major eligibility criteria; received at least two cycles of treatment, unless progression occurred before the second cycle, in which case the patients were considered to have progressive disease; had at least one complete tumor assessment after the second cycle; and had no major protocol violations. All patients who received at least one dose of study drug were assessable for safety assessment; safety analyses were performed based on the actual treatment administered.

Response rate was defined as the sum of the percentage of patients who achieved a complete response or partial response in each treatment group. Duration of response was defined as the time from the first documentation of response to the date of disease progression or the date of death as a result of any cause if death occurred within 1 month after the last dose of study drug. TTP was defined as the time interval between the date of random assignment and the date of disease progression or the date of death as a result of any cause if death occurred within 1 month after the last dose of study drug. For response duration and TTP analyses,
patients were censored at the time of last clinical contact if they were lost to follow-up, died later than 1 month after the last dose of study drug, or did not experience disease progression or die before the cutoff date for the analyses. Patients were also censored on the date that they received any subsequent anticancer therapy before documented tumor progression. OS was calculated from the date of random assignment to the date of death or to the date of last contact.

IV. RESULTS

Patients enrollment and baseline characteristics
A total of 170 previously untreated patients with advanced breast cancer (ABC) were enrolled onto this study between July 2023 to December 2023. Thirty patients were excluded because they did not meet the eligibility criteria and 140 patients were registered and 10 patients randomly assigned to ED, 10 patients randomly assigned to EP, 50 patients randomly assigned to DD and 50 patients assigned to DP. Five patients assigned to ED, 2 patients assigned to EP, 10 patients assigned to DD and 3 patients assigned to DP withdrew their consent before initiation of therapy and did not receive study treatment. 10 patients received ED, 10 patients received EP, 50 patients received DD and 50 patients received DP. The median age at randomization was 46 years (range 18-75 years). All baseline characteristics were well balanced between the four treatment groups.

Table 1. Baseline Patients characteristics

<table>
<thead>
<tr>
<th></th>
<th>ED</th>
<th>EP</th>
<th>DD</th>
<th>DP</th>
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</thead>
<tbody>
<tr>
<td>Patients</td>
<td>10</td>
<td>10</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.5 (18-75)</td>
<td>47 (19-75)</td>
<td>48.5 (21-76)</td>
<td>48 (20-76)</td>
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<tr>
<td>Menopausal status</td>
<td>2 20</td>
<td>1 10</td>
<td>8 16</td>
<td>12 24</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>8 80</td>
<td>9 90</td>
<td>42 84</td>
<td>38 76</td>
</tr>
<tr>
<td>Histological tumor type</td>
<td>5 50</td>
<td>5 50</td>
<td>27 54</td>
<td>30 60</td>
</tr>
<tr>
<td>Ductal</td>
<td>3 30</td>
<td>4 40</td>
<td>20 40</td>
<td>15 30</td>
</tr>
<tr>
<td>Lobular</td>
<td>2 20</td>
<td>1 10</td>
<td>3 6</td>
<td>5 10</td>
</tr>
<tr>
<td>Other</td>
<td>4 40</td>
<td>6 60</td>
<td>36 72</td>
<td>33 66</td>
</tr>
<tr>
<td>Prior treatment</td>
<td>5 50</td>
<td>6 60</td>
<td>35 70</td>
<td>33 66</td>
</tr>
<tr>
<td>Surgery</td>
<td>3 30</td>
<td>2 20</td>
<td>21 42</td>
<td>23 46</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>3 30</td>
<td>5 50</td>
<td>16 32</td>
<td>20 40</td>
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<tr>
<td>Hormonotherapy</td>
<td>4 40</td>
<td>5 50</td>
<td>20 40</td>
<td>11 22</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>4 40</td>
<td>6 60</td>
<td>36 72</td>
<td>33 66</td>
</tr>
<tr>
<td>Receptor status</td>
<td>4 40</td>
<td>6 60</td>
<td>36 72</td>
<td>33 66</td>
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</tbody>
</table>
Efficacy

The overall response rate was 60% (95% CI 50% to 70%) with ED versus 70% (95% CI 60% to 80%) with EP (p=0.80) and 34% (95% CI 30% to 38%) with DD versus 36% (32% to 42%) with DP (p=0.032). The median duration of response was 10.5 months on ED versus 10 months on EP and 10.5 months on DD versus 11 months on DP. The median TTP was 10 months on ED versus 11 months on EP and 8.5 months on DD versus 9 months on DP. The OS does not differ significantly between the ED was 36.7 and EP was 35.5 (p=0.03) two groups respectively. The OS slight differ in DD was 26 versus DP was 21 (p=0.013).

Table 2: Response, time to progression and overall survival

<table>
<thead>
<tr>
<th></th>
<th>ED</th>
<th>EP</th>
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<th>DP</th>
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<tbody>
<tr>
<td>Response</td>
<td></td>
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<tr>
<td>CR</td>
<td>2</td>
<td>2</td>
<td>13</td>
<td>10</td>
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<tr>
<td>PR</td>
<td>4</td>
<td>5</td>
<td>21</td>
<td>26</td>
</tr>
<tr>
<td>SD</td>
<td>3</td>
<td>2</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>PD</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Overall response rate % Patients</td>
<td>60</td>
<td>70</td>
<td>34</td>
<td>36</td>
</tr>
<tr>
<td>Duration of response Median, months</td>
<td>10.5</td>
<td>10</td>
<td>10.5</td>
<td>11</td>
</tr>
<tr>
<td>Time to progression Median, months</td>
<td>10</td>
<td>11</td>
<td>8.5</td>
<td>9</td>
</tr>
<tr>
<td>Overall survival (estimated) Median, months</td>
<td>36.7</td>
<td>35.4</td>
<td>26</td>
<td>21</td>
</tr>
</tbody>
</table>

Chemotherapy details

A total of 50 patients received 275 cycles of DD (mean, 5.5 cycles), 50 patients received a total of 280 cycles of DP (mean, 5.6 cycles), and 10 patients of each ED & EP received 60 cycles (mean, 6 cycles). Twelve patients received fewer than the maximum of six cycles of chemotherapy with DD because of toxicity (n=2), disease progression (n=1), with the reminder proceeding to surgery after fewer than six cycles at the investigator’s discretion (n=9). Ten patients received fewer than the maximum of six cycles of chemotherapy with DP because of toxicity (n=1), disease progression (n=2), with the reminder proceeding to surgery after fewer than six cycles at the investigator’s discretion (n=7). Similarly 2 patients received fewer than the maximum six cycles of chemotherapy with ED and EP because of toxicity (n=1), and investigator’s discretion (n=1).

Dose reduction was necessary with 36 cycles of DD (22%) in eleven patients, 38 cycles of DP(26%) in thirteen patients, 6 cycles of ED (20%) in two patients and 7 cycles of EP(20%) in two patients. In contrast, dose delay was necessary with 24 cycles of DD (14%) in seven patients, 27 cycles of DP (16%) in 8 patients, 9 cycles of ED& EP (30%) in three patients.

Toxicity

Toxicity of chemotherapy was recorded as the number of patients who experienced grade 3-4 toxicity shown in table. Hematological and non hematological toxic effects were generally mild and were similar in all treatment groups. Grade 3-4 leukopenia was observed in 2 patients (4%) with DD versus 1 (2%) with DP. Grade 3-4 neutropenia was observed in 2(20%) patients with ED versus 1 (10%) patient with EP (p=0.069) and 10 (20%) patients with DD versus 11 (22%) patients with DP (p=0.03). Grade 3-4 anemia occurred in 1 (10%) receiving ED versus 3 (30%) patients on EP (p=0.002) and 19 (38%) patients on DD versus 17 (34%) patients on DP (p=0.021). Hand foot syndrome grade 3-4 observed none of the group arm, no patients developed congestive heart failure. Non hematological toxicities were mostly grade 1-2. Grade 3-4 diarrhea toxicity was observed 4 (8%) on receiving DD versus 2 (4%) on DP and in one patients on ED. Neurotoxicity grade 3-4 was observed none of the patients with ED and EP but 1 (2%) patient on DD versus 3 (6%) patients on DP (p=0.022) was observed.

Table 3. Grade 3 and 4 Toxicity Recorded As the Number of Events for All Cycles of Chemotherapy

<table>
<thead>
<tr>
<th>Toxicity grade</th>
<th>ED n</th>
<th>EP %</th>
<th>DD n</th>
<th>EP %</th>
<th>DD n</th>
<th>EP %</th>
<th>DP n</th>
<th>EP %</th>
</tr>
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<tbody>
<tr>
<td>3-4</td>
<td></td>
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</table>
V. DISCUSSION

Anthracyclines and taxanes are recommended for the adjuvant treatment of women with operable advanced breast cancer. Several regimens are being used by clinicians, including standard dose sequential, concurrent and dose-dense sequential [10]. The combination of anthracyclines (Epirubicin, doxorubicin) and taxanes (docetaxel, paclitaxel) has demonstrated significant activity as first-line chemotherapy in ABC. The rationale for combining taxanes with anthracyclines rests on a number of observations. Individually they have the greatest single agent activity in and have largely non-overlapping patterns of commonly encountered adverse events [11]. The primary objective of this study, which was to show a large superiority in TTP, ORR, OS for the ED regimen compared with EP and DD regimen compared with DP, was not met; the study lacks power to rule out smaller differences. Nevertheless, our results indicate that the activity and efficacy of the two regimens as first line therapy are similar in terms of overall survival rate, durations of response, TTP and OS. The clinical response rates with ED (60%), EP (70%), DD (34%), and DP (36%) reported here are comparable to the overall clinical response rates reported in some previous study---. There is no significant difference in quality of life scores between the ED versus EP and DD versus DP. Non-hematological toxicity was significantly more frequent in arm DD, as well as grade 3-4 mucositis. Neurotoxicity occurred more frequently in arm DP as compared to arm DD. The efficacy results are shown in table 2, and demonstrated that the paclitaxel or docetaxel combination with doxorubicin was not significantly different in terms of quality of life scores and efficacy, but had different toxicity profiles[12]. The median duration of response (10-11 months), TTP (8-11 months) and OS (21-36 months) in our trial are very acceptable for patients with an incidence of visceral metastases of approximately 65% and a high rate of adjuvant chemotherapy, including anthracyclines. Furthermore, the results are very similar to those found in other studies using a conventional 3-week schedule[13]. This study does not support the proposed relationship of tumor oxygenation and sensitivity to cytotoxic agents. In the mean time studies, have raised concerns about inferior long-term outcomes if erythropoietin-stimulating agents were used to increase hemoglobin but not if the intention was to prevent severe anemia.[14]. The rational behind this choice was centred on the dose-density theory based on the reduction of the intervals between chemotherapy doses to restrict the opportunity for cancer cells to become resistant to drugs and to target cell clones with differing growth rates. Furthermore, weekly administration of chemotherapy in a dose-dense schedule is understood to have an antiangiogenesis effect, constricting the blood supply to tumours and restricting their growth. Thus, the weekly schedule was designed to allow administration of a total dose of drug greater than or equal to that administered with the conventional 3-week schedule, to enhance cumulative cytotoxic activity while reducing the toxicity of the treatment, providing greater therapeutic benefit together with a more favourable tolerability profile [15-17]. This study has limitations due to its small sample size; which should be mentioned. The sample size is not large enough to detect a small but clinically meaningful difference even it was originally calculated to have sufficient power for DFS and pCR. Treatment duration and drugs of the four chemotherapy arms are not completely identical.

VI. CONCLUSION

This multicenter randomized study indicates that the DD and DP regimens have similar efficacy but different toxicity as first line treatment of ABC and in ED &EP regimen is difficult to compared the efficacy and toxicity because of small sample size. Until individualized therapy becomes a reality in everyday clinical practice, either regimen can be used for the treatment of women with HER2-negative ABC who due to aggressive disease might benefit from combination chemotherapy.

REFERENCES


