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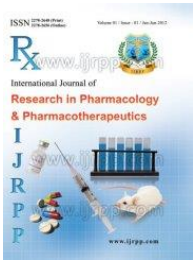

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Research article ***Open Access***

Drug utilization review and quality of life of biosimilars used in oncology in tertiary care hospital

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ABSTRACT

Background
Biosimilars are considered to be one of the solutions to combat the substantially increasing costs of cancer treatment and its imminent introduction is expected to expand affordability worldwide. Biosimilars were developed as copies of original products that were themselves copies/better biosimilars of natural proteins.

Objectives
To review the drug utilization and Quality of life of biosimilars used in oncology patients.

Methods
It was a Hospital based observational, prospective study conducted by random selection of 50 patients. The data was collected regarding demographic details of the patient, chemotherapeutic drugs and administration,diagnosis, laboratory tests, mammography, PET (positron emission tomography), present complaints, history of patients and QOL of patients were also recorded. Patients were included in the study after obtaining verbal informed consent.

Results and discussion
In this prospective observational study the drug utilization review of biosimilars in various types of cancers were evaluated in a total of 50 patients.Among 50 patients who were treated with biosimilars and chemotherapeutics, 22% were male and 78% were female. The mean total scores for breast cancer, lung cancer, melanoma,NHL ,HL Urothelial carcinoma and colon cancer subjects at final visit increased compared to initial visit. This increment was highly significant statistically and the values were found to be [t= 30.9487, p= 0.0001] at 95% confidence interval.

Conclusion
All biosimilars showed improvement in symptoms &QOL scores. During the study period it was revealed that the most commonly used biosimilars for breast cancer was Trastuzumab, lung cancer durvalumab, melanoma & hodgkin's lymphoma & urothelial carcinoma & colon cancer nivolumab, non-hodgkin's lymphoma rituximab. The maximum improvement in QOL was obtained with nivolumab in urothelial cancer, melanoma &Hodgkin's lymphoma patients.

Keywords: Biosimilars, Cancer, Fact Questionnaire, QOL, DUR.

INTRODUCTION

Biosimilars are important components of the modern cancer treatment armamentarium [1] and are recommended for the treatment of various types of cancers by National Comprehensive Cancer Network (NCCN) and American Society for Clinical Oncology (ASCO) guidelines because they improve clinical outcomes, including overall survival (OS) [2, 3].

According to a 2011 drug expenditure analysis, biologics accounted for approximately 55% of the total expenditure on antineoplastic drugs in the US health care system; among the biologics, bevacizumab (Avastin; Roche, Basel, Switzerland), rituximab (Rituxan/MabThera; Roche), and trastuzumab (Herceptin; Roche) accounted for more than half of the top 20 antineoplastic expenditures in outpatient clinics [1, 2, 4, 5]. Bevacizumab is approved for the treatment of colorectal, brain, lung, fallopian tube, renal, and other cancers [6]; rituximab is approved for the treatment of CD20-positive non-Hodgkin lymphoma and leukemia [7]; and trastuzumab is approved for the treatment of human epidermal growth factor receptor 2 (HER2) –positive breast cancer and metastatic gastric and gastroesophageal junction adenocarcinomas [8].

Similarly, the European Union defines a biosimilar medicine as a medicinal product, which is a copy of a biologic product (the reference product) that has already received authorization [9]. Biosimilars are also referred to as follow-on biologicals, similar biotherapeutic products, or subsequent-entry biologics [10]. The term biogenerics is also used occasionally but should be avoided because it may imply that biosimilars are identical to the original compounds, as in the case of generic versions of small-molecule drugs [9].

Efficacy and safety of some biosimilars have also been tested in real-world settings with encouraging results [11]. Such studies have prompted regulatory bodies to adopt a more positive opinion of biosimilars, even in highly regulated markets, paving the way for future inclusion of biosimilars in oncology therapy [12].

BIOSIMILARS IN ONCOLOGY

Canmab-Trastuzumab

Composition:-150mg single dose and 440mg multi dose vials containing powder for concentrate for solution for intravenous solution.

Dilution:- 440mg of trastuzumab in 500ml of Normal saline for 2 hours.

Abevmy-Bevacizumab

Composition:-100mg in 4ml vial contains 100mg of bevacizumab concentrate for solution for intravenous infusion.

400mg in 16ml contains 400mg of bevacizumab concentrate for solution for intravenous infusion.

Dilution:-Abevmy 100mg solution is supplied in single use vial containing 100mg {25mg/ml)of bevacizumab ,23.20 mg of monosodium phosphate monohydrate IP,4.80 mg of disodium phosphate anhydrous ,960mg of Rehalose dihyadrate,160mg of polysorbate 20 IP and water for injection [IP].

400mg solution is supplied in a single-use vial containing 400mg [25mg/ml]of bevacizumab,92.80mg of monosodium phosphate monohydrate IP,19.20 mg of disodium phosphate anhydrous,960mg of trehalose dehydrate,6.40mg of polysorbate 20IP and WFI.

Imfizni-Durvalumab

- Composition-each ml of solution contains 5omg durvalumab concentrate solution as active substance.
- Each vial contains 120ml /2.4ml[50mg/ml]single dose vial
- 500mg/10ml [50mg/ml] single dose vial.
- Dilution:-diluted in 250 ml of saline for 2 hours.

Opdyta-Nivolumab

- Composition:-one vial of 4ml contains 40mg of nivolumab.
- onevial of 10ml contains 100mg of nivolumab.
- Dilution:-280mg of nivolumab in 160ml of normal saline for 30 minutes.

Mabthera-Rituximab

- Composition:- 10mg/ml[100mg/10ml or 500mg/50ml single dose vials]
- Dilution:-500mg of rituximab in 250ml of normalsaline.

DUR

It is an on-going,authorized,and systemic quality improvement process which is designed to:

- Review the drug use and prescribing patterns
- Provide the feedback of results to clinicians& the relevant groups
- Develop criteria&standards which describes the optimal drug use
- Improve the prescriber awareness and practice towards appropriate prescribing.

QUALITY OF LIFE

Health-related quality of life (HRQOL) is a multi-dimensional concept that includes domains related to physical, mental, emotional and social functioning. Clinicians and public health officials have used HRQOL and well-being to measure the effects of chronic illness, treatments and short and long-term disabilities.

Functional Assessment of Cancer Therapy (FACT) Questionnaire

The FACT questionnaire has four main domains to analyse and interpret the Quality of Life and well-being of the patients. The domains include:

- Physical well-being.
- Social/Family well-being.
- Emotional well-being.
- Functional well-being.

METHODOLOGY

This prospective ,observational study collected demographic,diagnostic,and therapeutic data from 50 cancer patients. The study was carried out for 6months duration in 0ncology In Patient and Day care Department. A multidisciplinary palliative care team using the Functional Assessment of Cancer Therapy-General (FACT-G©) questionnaire.

STATISTICAL ANALYSIS

The data collected was analysed with the following criteria- level of significance was fixed at $p<0.0001$ with 95% confidence interval. The *Paired t- test* was used and all statistical calculation was carried out with GraphPad QuickCalcs: t test calculator: A web based statistical calculator [13].

RESULTS

Table 1- Distrubution of Patients Based on Gender

SEX	MALE	FEMALE
NO. OF PATIENTS(%)	11(22%)	39(78%)

Table 2:- Distribution of Patients Based on The Age Groups

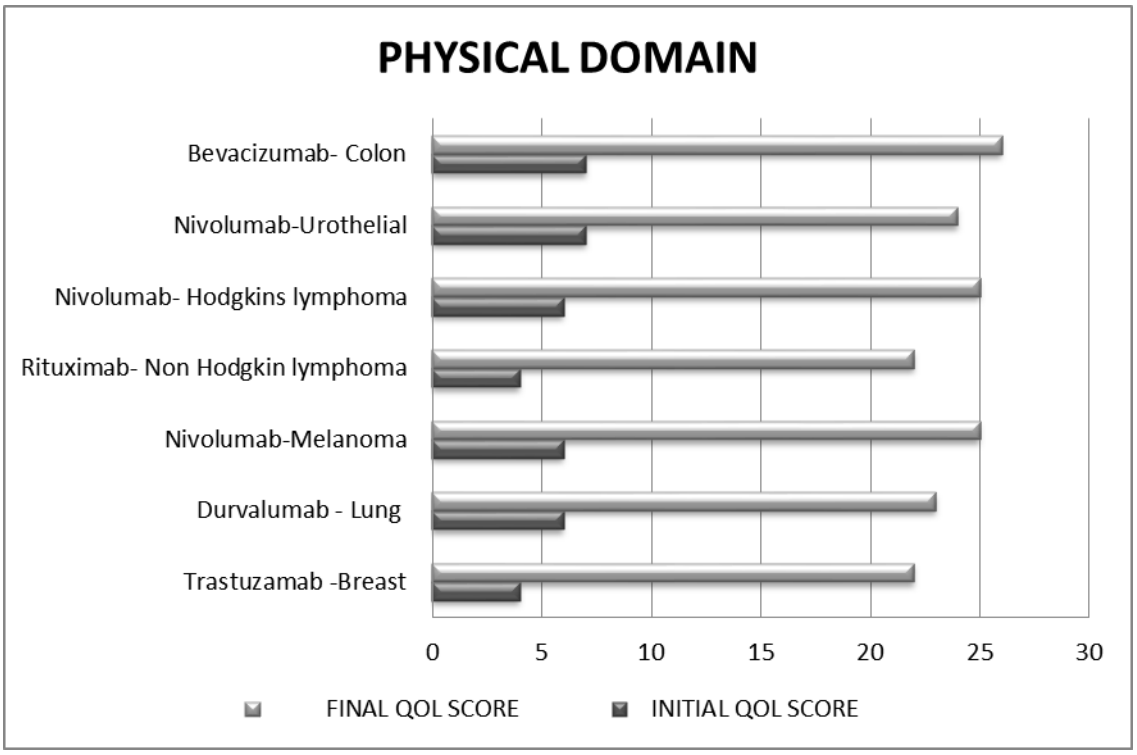
AGE(Yrs)	26-35	36-45	46-55	56-65	66-75	76- 85
MALE	0	1	2	4	4	0
FEMALE	2	9	14	9	3	2

Table 3: distribution of patients based on types of cancers

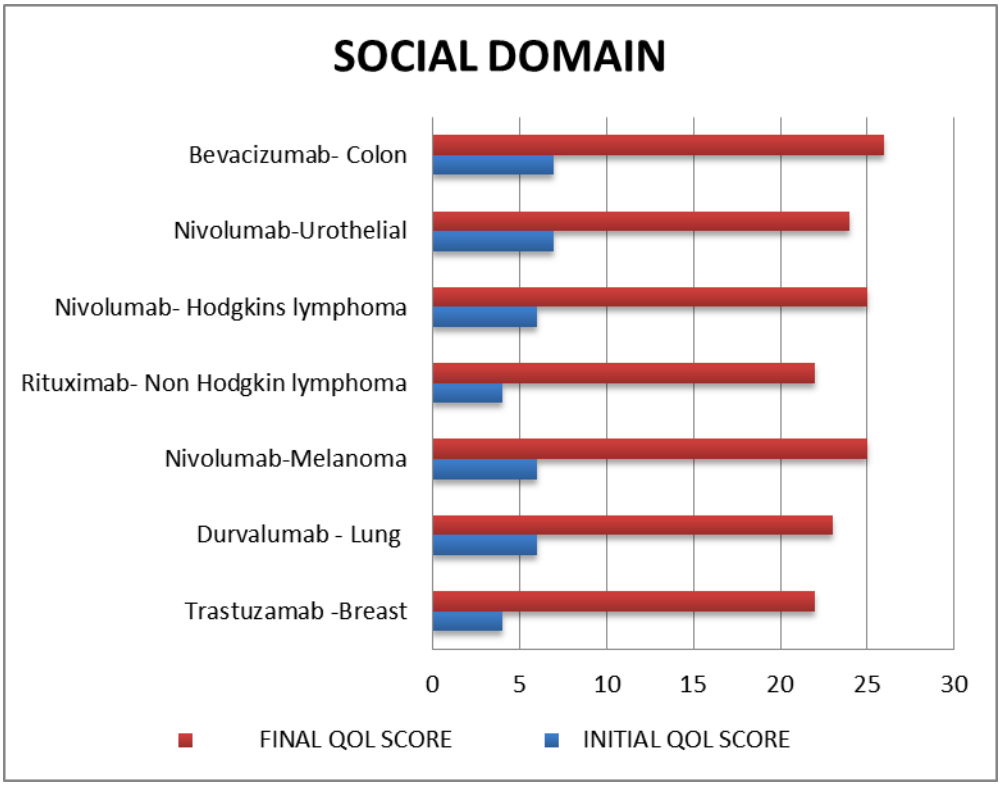
CANCER	PATIENTS	PERCENTAGE
BREAST CANCER	34	68%
LUNG CANCER	5	10%
COLON CANCER	3	6%
HODGKIN'S LYMPHOMA	2	4%
NON-HODGKINS LYMPHOMA	2	4%
MELANOMA	3	6%
UROTHELIAL CARCINOMA	1	2%
Total	50	100%

Table 4: Different Categories of Drugs Used Prior to Biosimilars

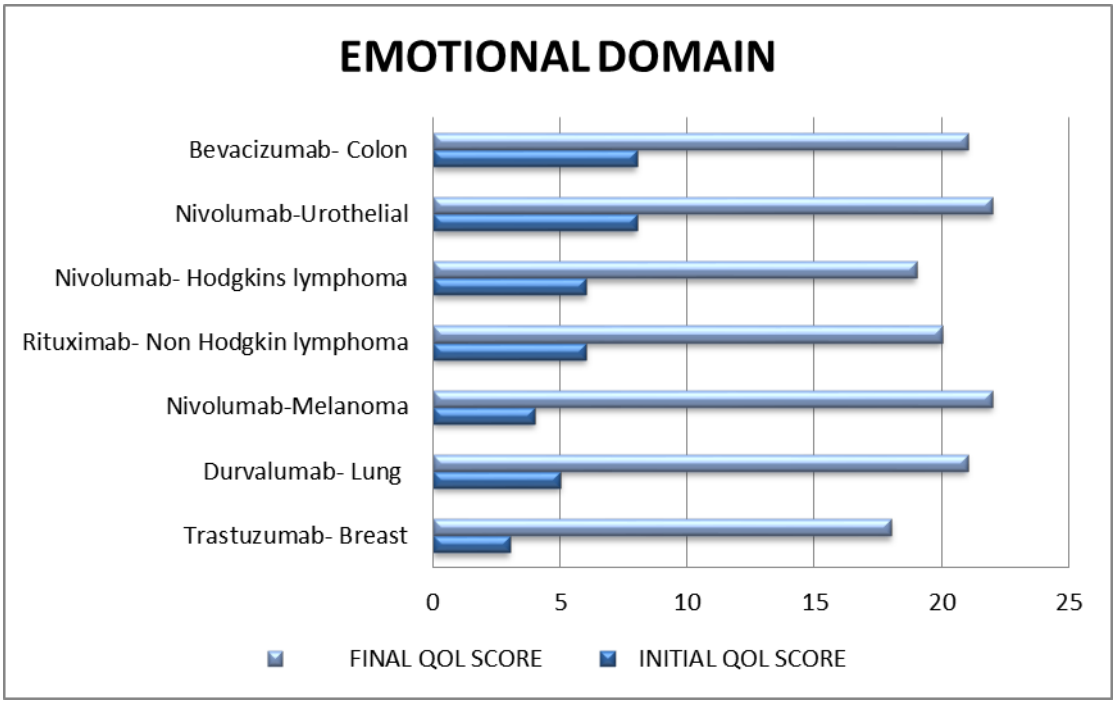
S.NO	CATEGORY	CLASS	DRUGS
1.	**Anti-neoplastic (cytotoxic drugs)**	Microtubule damaging agent	Docitaxel ,vincristine
		Platinum co-ordination complexes	Carboplatin, Cisplatin
		anthracycline antibiotics	Famorubicin , Adriamycin
		Topoisomerase -1 inhibitor	Etoposide
		Nitrosureas	Bendamustine
		Nitrogen mustards (alkylating agents)	Cyclophosphamide
2.	**Hormonal drugs**	Selective estrogen receptor down regulators	fulvestrant
3.	**Anti- metabolites**	Folate antagonist	Methotrexate, Pemetrexed
4.	**GCSF(granulocyte colony stimulating factor)**	Hematopoietic growth factor	Peg filgrastin



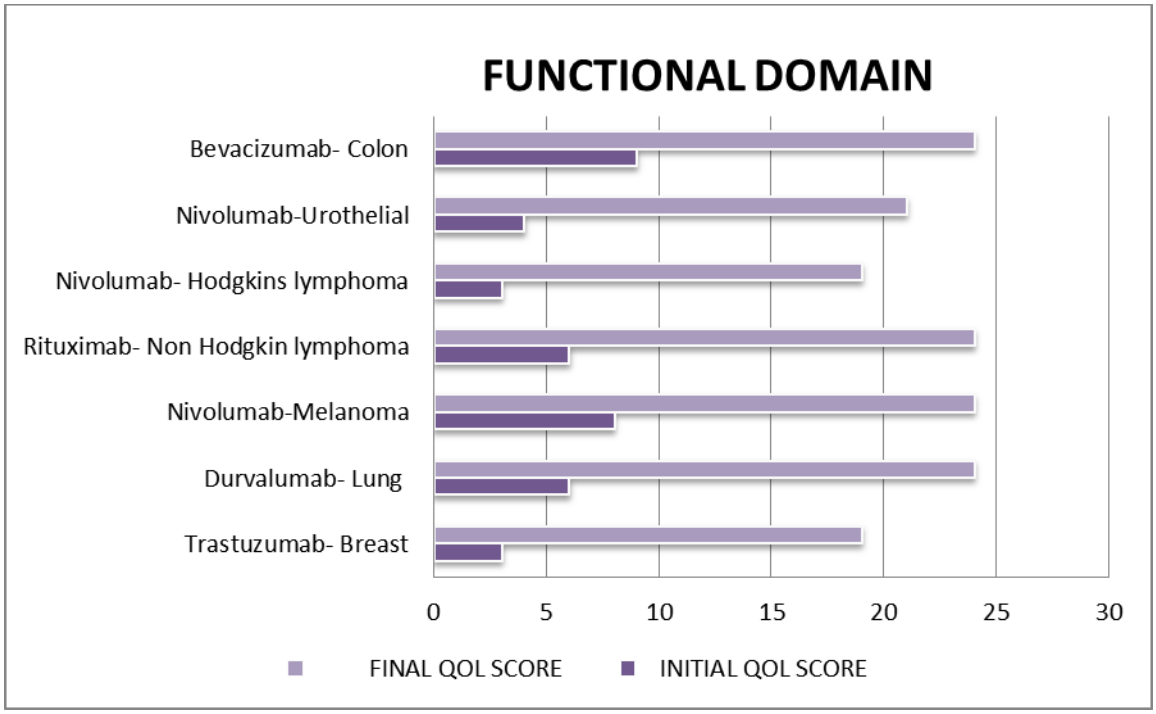
Graph 1: **Physical Domain**



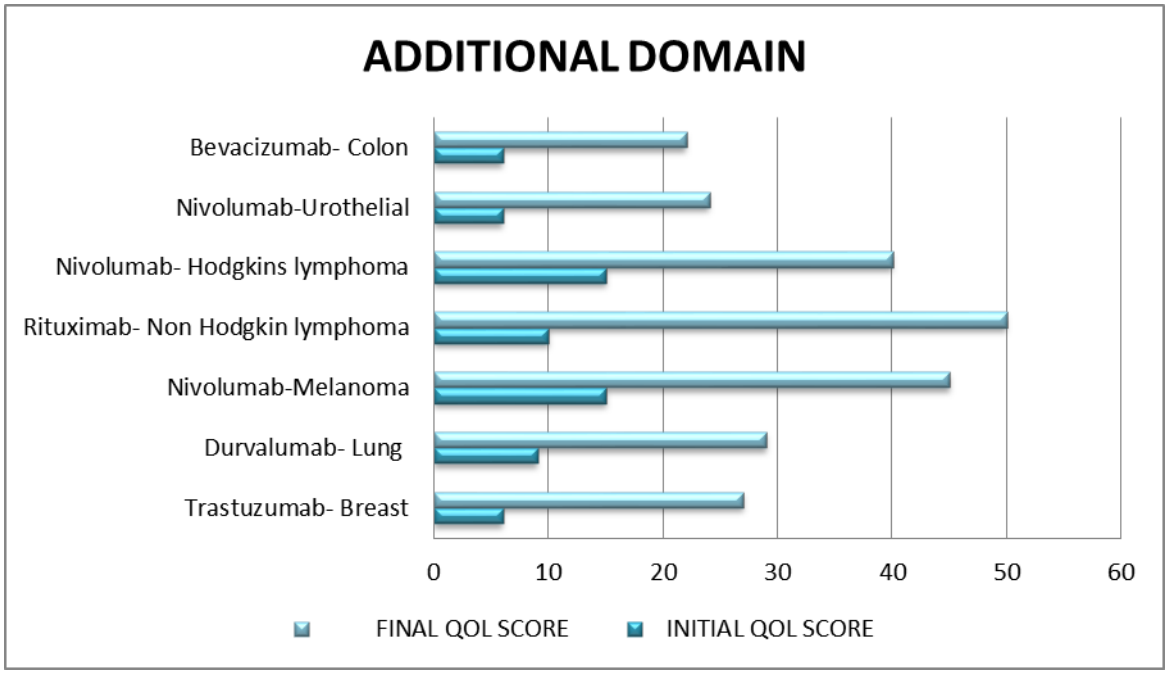
Graph2: **Social Domain**



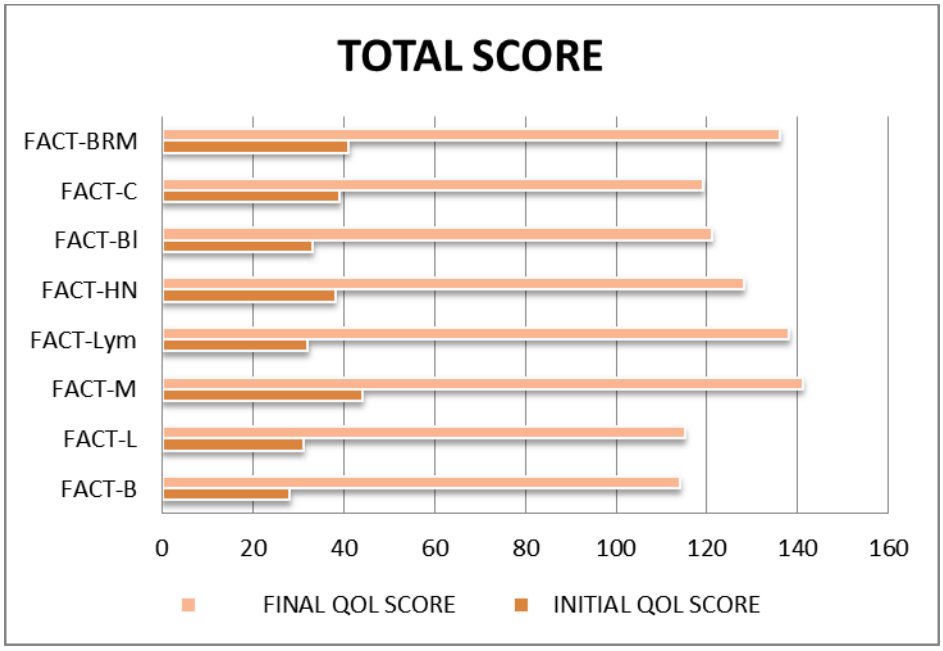
Graph3: **Emotional Domain**



Graph4: **Functional Domain**



Graph5 **: Additional Domain**



***Graph6* : Total Score**

Among 50 patients, 22% were male and 78% were female. The age of patients who were included in the study ranged from 26-85years and maximum patients who were admitted to the hospital were of the age group 46-55years. During the study period it was revealed that 95% of the total patients have come out with favourable treatment outcomes based on subsiding of symptoms with respect to biosimilars whereas 5% of the patients hesitated to answer the questionnaire because of which outcome cannot be predicted. The study revealed that the number of patients diagnosed from breast cancer was high. The study also revealed that Trastuzumab and nivolumab were the mostly prescribed biosimilars for most of the patients because of their targeted action these drugs were prescribed with the combination of other chemotherapeutics such as paclitaxel which is a mitotic inhibitor, used for breast carcinoma for 25% of the breast cancer patients and docitaxel for 28% of total patients.

The mean additional concerns domain score for breast cancer, lung cancer, melanoma, NHL ,HL Urothelial carcinoma&colon cancer subjects at initial visit was ,**BC-6 ,LC-9,ML-15,NHL-10, HL-15, UC-6 ,CC-6**and scores increased to **BC-27, LC-29,ML-45 ,NHL-50,HL-40, UC-24 ,CC-22** at final visit**..** This increment was highly significant statistically and the values were found to be [t= 7.7034, p= 0.0003] at 95% confidence interval.

The mean total score for breast cancer, lung cancer, melanoma, NHL ,HL Urothelial carcinoma& colon cancer subjects at initial visit was , **FACT-B:28, FACT-L:31, FACT-ML:44, FACT-Lymph:32,FACT-HN:38, FACT-BI:33, FACT-C:39 –FACT-BRM:41**and scores increased to **FACT-B:114, FACT-L:115, FACT-ML:141 ,FACT-Lymph:138,FACT-HN:128, FACT-BI:121 ,FACT-C:119 –FACT-BRM:136** at final visit**..**This increment was highly significant statistically and the values were found to be [t= 30.9487, p= 0.0001] at 95% confidence interval.

CONCLUSION

Our study demonstrates that FACT-G is useful outcome for QOL measures in oncology studies & is able to measure dimensions not measured by diagnostic tests that help to identify subtle differences between biosimilars. All biosimilars showed improvement in symptoms & QOL scores. The maximum improvement in FACT-QOL (P<0.0001) was noted in patients receiving biosimilars with respect to FACT (physical, social, emotional, functional and additional domains) scores with trastuzumab in breast cancer, bevacizumab in colon cancer, rituximab in non-hodgkin's lymphoma,

durvalumab in lung cancer, nivolumab in urothelialcancer, melanoma & Hodgkin's lymphomapatient's. More studies comparing different cancer specific questionnaires as Quality of life of Cancer Patient's [QOLCP]questionnaire, European organisation for research and treatment of cancer [EORTC]questionnaire all necessary to identify ideal HRQOL measure in cancer.

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