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Research article

Real-world drug treatment models of novel targeted drugs in Chinese patients with gynecological cancer from 2017 to 2021: A cross-sectional analysis

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ABSTRACT

Objective: The significance of novel anti-tumor pharmaceuticals in the treatment of gynecological tumors is growing, but there is no consensus regarding the optimal drug delivery strategy for gynecological tumors. This study seeks to investigate the treatment models of novel anti-tumor drugs in patients with gynecological cancer in China over the past five years, with a particular emphasis on the trend and rationality of their use.

Method: We conducted a cross-sectional analysis of data from a China Medical Association-supervised hospital prescription analysis cooperation initiative. The data was derived from prescriptions written for patients diagnosed with cancer between January 2017 and December 2021. The required information for patients was extracted. Our study included 2308 patients that were diagnosed as gynecological tumors which were treated with novel antineoplastic targeted drugs. Patients were categorized by age and region. Then, the selection, application, and indications of the most essential treatment pharmaceuticals were investigated. We evaluated anti-tumor prescription information based on the recommended drug labeling protocol and the most recent domestic and international guidelines.Excel 2013 and SPSS (version 25; SPSS Inc., Chicago, IL, United States) were utilized to conduct statistical analysis.In addition , we also used Sankey diagram to evalute the relation between novel antineoplastic targeted drugs and corresponding diagnoses.

Result: The top three cities for the 2308 patients included in this study were Guangzhou (28.51%), Hangzhou (21.79%), and Beijing (20.06%). In the past five years, the average age of medication patients was 55.61-year-old, with 37.86% of women aged of 51–60. Each patient's primary treatment regimens were statistically analyzed, yielding a total of 16 single-drug and combination-drug primary treatment regimens. Bevacizumab, Olaparib, Trastuzumab, Apatinib, and Arotinib were the top five treatment strategies. The maximum proportion, up to 0.74%, was attributed to the combination of human epidermal growth factor receptor-2 inhibitor (HER2i), including Trastuzumab and Parostuzumab. Vascular endothelial growth factor receptor inhibitor (VEGFRi), including Bevacizumab and Apatinib was the most frequently prescribed medication for outpatients in major cities across the country. According to the 5-year change in time, poly adenosine diphosphate ribose polymerase inhibitor (PARPi) rated first in terms of usage, with Olaparib ranking first with the highest concentration of 33.44% and Niraparib ranking second overall with the fastest growth in 2021. The quantity of VEGFRi variants utilized was the greatest,

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and their proportion of total usage increased annually. The top five drugs by total drug costs were Bevacizumab, Carelizumab, Olaparib, Trastuzumab, and Apatinib. However, the top five drugs by per capita drug cost were Olaparib + Bevacizumab, Bevacizumab + Sidilimab, Arrotinib + Olaparib, Olaparib, and Patuzumab + Trastuzumab.

Conclusion: The incidence rate of gynecological tumor patients rises with age, and the cost of drug treatment has risen annually over the past five years, which is also related to the rising incidence rate of tumors in recent years. Bevacizumab rates first in the drug treatment scheme for the application of novel anti-tumor targeted drugs, which may be related to the widespread use of VEGFRi drugs in gynecological and reproductive tumors. Breast cancer and adenocarcinoma are at the top of the female cancer incidence spectrum, which may explain why HER2i multi-drug combination regimen rates highest among multi-drug combination regimens. Future research may concentrate on how novel anti-tumor targeted drugs can minimize the economic burden and maximize the benefits of patient treatment for patients with gynecological cancer.

1. Background

In recent years, the incidence rate of gynecological malignancies has increased annually, posing a grave threat to the life and health of women. The most prevalent gynecological malignancies are cervical cancer, endometrial cancer, and ovarian cancer, among others [1]. According to the 2020 Global Cancer Statistics Report, there were 604,000 cases of cervical cancer, 417,000 cases of endometrial cancer, and 314,000 cases of ovarian cancer, correspondingly, with 342,000, 97,000, and 207,000 deaths in global [2]. In addition, female breast cancer surpassed lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3 million new cases, representing 11.7% of all cancer cases.It was the fifth leading cause of cancer mortality worldwide, with 685,000 deaths [2]. According to the 2015 China Cancer Incidence and Death Statistics Report, the incidence rates of cervical cancer and endometrial cancer were sixth and eighth respectively among female malignant tumors in China [3]. For women, among the 10 most common types of cancer, death rates increased in breast cancer, cervical cancer and ovarian cancer [4]. The prevention and treatment of gynecological malignant tumors are still challenging.

Malignant tumor treatment continues to be a significant clinical problem that the world's medical community is working to address. Tumor treatment options currently include surgery, radiation therapy, and medication therapy. Traditional surgical resection is difficult to complete, resulting in postoperative recurrence. Traditional chemotherapy medications and radiotherapy kill not just tumor cells but also normal cells, inflicting severe harm to patients [5]. The development of novel anti-tumor treatments, such as molecular targeted therapies, immunotherapy drugs, new formulations of classic chemotherapy drugs, and multitarget new anti-tumor drugs, has given people renewed hope. Tumor targeted therapy, which has great efficacy and few side effects, intervenes in the excessive proliferation, infiltration, and metastasis of tumor cells through corresponding target selection. With the continual release of targeted medications in recent years, cancer patients' survival times have been greatly extended, as has their quality of life. A vast number of studies have revealed that immunotherapy has incomparable advantages over traditional anti-tumor therapy, such as extending progression-free survival and overall survival, having good anti-tumor efficacy, having minimum adverse responses, and reducing recurrence [6].

In China, there are limited studies on the use of novel anti-tumor medications in gynecological cancer patients. How to apply novel targeted medications responsibly and generate standard evaluation indicators is becoming an increasingly important problem for tumor specialists to consider in clinical practice. By examining real-world data from 2017 to 2021, we want to close this knowledge gap.In this study, we studied the specific use of these prescribed new antitumor drugs that included the demographic characteristics and the types of drugs used by patients, the relationship between drug use and diagnosis, and the treatment costs of patients so that we can find out the rules and provide reference for the treatment of gynecological tumors.

2. Methods

The China Medical Association's hospital prescription analysis cooperation project collected prescription data from over 120 hospitals in Beijing, Chengdu, Guangzhou, Harbin, Hangzhou, Shanghai, Shenyang, Tianjin, and Zhengzhou on a quarterly basis from 2017 to 2021. The following information was provided by this project: Time, city, hospital code, common name joint plan, age, initial diagnosis, prescription ratio, proportion of patients, and amount were all variables to consider.

This study extracted the outpatient prescription data of women diagnosed with gynecological tumors and treated with new targeted anti-tumor drugs (such as Bevacizumab, Trastuzumab, Enmetrastuzumab, Patuzumab, Inistumab, Lapatinib, Pyrrolitinib, Nelatinib, Piperacillin, Olaparib, etc). Immunotherapeutic drugs were included among the involved drug categories. The diagnosis included gynecological tumors and their recurrence, as well as the diagnosis of gynecological tumors combined with other tumors, such as "ovarian cancer", "ovarian cancer recurrence", "cervical cancer", "breast cancer", "gestational trophoblastic tumor", "malignant tumor of the fallopian tube", etc., and excluded patients with incomplete diagnosis that didn't include diagnosis of gynecological tumors, such as "myelosuppression", "thrombocytopenia".

For additional analysis, we divided patients into different age groups and geographic regions, screened the most important treatment medications, and conducted additional analysis based on drug treatment plans, patient age factors, disease diagnosis, rationality, etc. According to the pharmacological classification of the principal therapeutic drugs, the sales volume of the drugs

consumed in the previous two years is computed, and the proportion of sales volume to total sales volume was categorized. Simultaneously, we analyzed the patient's diagnosis in conjunction with the clinical medication situation and drug instructions. To conduct a rationality analysis, we evaluated anti-tumor prescription information based on the recommended drug labeling protocol and the most recent domestic and international guidelines.Excel 2013 and SPSS (version 25; SPSSInc., Chicago, IL, United States) were utilized to conduct statistical analysis. Continuous variables were represented by their mean standard deviation. Presenting categorical variabled as numbers and percentages. Demographic and prescription information was grouped into counts.

3. Results

3.1. Demography characteristics of patients

In accordance with the inclusion criteria, we included prescription data for 2308 patients, such as region, age, cost, etc. Guangzhou (28.51%), Hangzhou (21.79%), and Beijing (20.06%) were the top three cities. Over a five-year period, the average age was 55.61-year-old, with approximately 63.73 percent of women over the age of 51-year-old, and the cost of medication increased progressively. Table 1 lists the demographic characteristics of patients.

3.2. Types of medication used by patients

We examined the study patients' key therapy medications, namely single drug regimens and combination regimens, such as VEGFRi, PARPi, HER2i, programmed death-l inhibitor (PD-1i). With a total proportion of 98.21%, there are 11 single medication regimens and 5 combination regimens. The top five are VEGFRi (879, 38.08%), PARPi (698, 30.24%), HER2i (346, 14.99%), epidermal growth factor receptor (EGFRi) (233, 10.10%), and PD-1i (96, 4.16%); the total proportion of combined medication regimens is 1.79%, with HER2i (17, 0.74%), EGFRi + PARPi (9, 0.39%), and VEGFRi + PARPi (8, 0.35%). Table 2 depicts the corresponding type distribution. Subgroup analysis on single medication regimen and combined regimen was performed to further investigate drug modifications, as shown in Table 3. Bevacizumab accounted for 28.26% of the first place in the single drug scheme, with the fastest rising trend in five years, followed by Olaparib, which ranked second in total amount, with a total proportion of 25%, and consumption increased rapidly in recent years; Trastuzumab, ranking third, has been used repeatedly in the past five years.

3.3. Patient medication diagnosis chart

We summarized the top ten medications and their corresponding diagnoses, and found that drugs corresponding to ovarian cancer (including recurrence) accounted for the greatest number, followed by cervical cancer and breast cancer. See Fig. 1 for details.

3.4. Costs

Patients' total and per capita costs for treatment medications were calculated. The top five drugs by total cost were Bevacizumab, Olaparib, Apatinib, Nituzumab, Trastuzumab + Patuzumab; the top five drugs by per capita cost are Olaparib + Bevacizumab, Bevacizumab + Cindilimab, Arotinib + Olaparib, Olaparib, and Arotinib + Niraparib. For more information, see Table 4.

Table 1
Demographic characteristics of the patients ($n = 2308$).

Year	2017	2018	2019	2020	2021	Tatol
Region, n (%)						
Beijing	12 (2.57%)	33 (7.28%)	40 (8.78%)	135 (29.12%)	243 (52.25%)	463 (20.06%)
Chengdu	0 (0.00%)	1 (12.5%)	0 (0%)	3 (37.5%)	4 (50%)	8 (0.35%)
Guangzhou	47 (7.14%)	59 (8.97%)	41 (6.23%)	130 (19.76%)	381 (59.90%)	658 (28.51%)
Haerbin	0 (0.00%)	0 (0.00%)	4 (22.22%)	5 (27.78%)	9 (50.00%)	18 (0.78%)
Hangzhou	1 (0.20%)	55 (10.93%)	128 (25.45%)	130 (25.84%)	189 (37.58%)	503 (21.79%)
Shanghai	20 (5.52%)	37 (10.22%)	36 (9.94%)	113 (31.22%)	156 (43.10%)	362 (15.68%)
Shenyang	0 (0.00%)	0 (0.00%)	1 (17.24%)	7 (12.07%)	50 (70.69%)	58 (2.51%)
Tianjin	0 (0.00%)	0 (0.00%)	0 (0.00%)	11 (28.21%)	28 (71.79%)	39 (1.69%)
Zhengzhou	0 (0.00%)	5 (2.51%)	18 (9.04%)	46 (23.12%)	130 (65.37%)	199 (8.62%)
Tatol	80 (3.47%)	190 (8.23%)	268 (11.61%)	580 (25.13%)	1190 (51.56%)	2308 (100%)
Drug costs (RMB)	434417.32 (2.23%)	1192002.12 (6.13%)	1815465.97 (9.33%)	5840003.65 (30.02%)	10168871.47 (52.29%)	19450760.53 (100%)
Age, n (%)						
18-24	3 (3.75%)	0 (0.00%)	0 (0.00%)	1 (0.17%)	3 (0.25%)	7 (0.30%)
25-34	13 (16.25%)	10 (5.26%)	5 (1.86%)	11 (1.90%)	17 (1.43%)	56 (2.42%)
35-44	10 (12.50%)	24 (12.63%)	45 (16.79%)	57 (9.83%)	113 (9.49%)	249 (10.79%)
45-50	13 (16.25%)	35 (18.42%)	45 (16.79%)	100 (17.24%)	184 (15.46%)	377 (16.33%)
51-60	19 (23.75%)	51 (26.84%)	85 (31.72%)	178 (30.69%)	393 (33.02%)	726 (31.45%)
> 60	18 (20.00%)	62 (32.63%)	84 (31.34%)	181 (31.20%)	400 (33.61%)	745 (32.28%)
Average	54.71	55.60	55.62	55.66	55.55	55.61

Table 2
Main drug therapeutic regimens of the patients (n = 2308).

Treatment methods	Classification	Treatment plan	2017	2018	2019	2020	2021	Tatol	Mean age
Monotherapy	PARPi	Olaparib、Niraparib	–	–	–	197 (33.22%)	501 (41.20%)	698 (30.24%)	57.58 ± 9.15
	VEGFRi	Bevacizumab、Apatinib	40 (50.00%)	121 (63.68%)	118 (44.02%)	198 (33.72%)	402 (32.98%)	879 (38.08%)	56.45 ± 9.92
	EGFRi	Anlotinib、Nituzumab、Lapatinib、Gefitinib、Qsimertinib	–	18 (9.47%)	29 (10.82%)	78 (13.08%)	108 (9.61%)	233 (10.10%)	53.00 ± 12.99
	HER2i	Trastuzumab、Pertuzumab、Initumab	–	51 (26.85%)	119 (44.40%)	85 (16.61%)	91 (9.04%)	346 (14.99%)	52.43 ± 9.75
	PD-1i	Sindillimab、Carrilizumab、Triplimab、Tirellizumab	40 (50.00%)	–	–	9 (1.17%)	47 (3.83%)	96 (4.16%)	50.15 ± 10.46
	mTORi	Everolimus	–	–	–	2 (0.33%)	6 (0.49%)	8 (0.35%)	67.25 ± 9.65
	VEGFRi	Renvastinib	–	–	–	–	3 (0.24%)	3 (0.13%)	60.33 ± 0.47
	ALK、MET、ROS1i	Crizotinib	–	–	–	–	2 (0.16%)	2 (0.09%)	48.00 ± 18.00
	PDGFRi	Imatinib	–	–	1 (0.19%)		10.08%)	2 (0.09%)	51.50 ± 12.50
	MEKi	Trametinib	–	–	–	–	1 (0.08%)	1 (0.04%)	42.00 ± 0.00
	TKi	Dasatinib	–	–	1 (0.19%)	–	–	1 (0.04%)	56.00 ± 0.00
Combined administration	HER2i	Trastuzumab + Pertuzumab	–	–	–	7 (1.17%)	10 (0.81%)	17 (0.74%)	42.00 ± 0.00
	EGFRi + PARPi	Anlotinib + Olaparib、Anlotinib + Niraparib	–	–	–	–	9 (0.73%)	9 (0.39%)	
	VEGFRi + PARPi	Bevacizumab + Olaparib、Renvastinib + Olaparib、Apatinib + Olaparib、Apatinib + Niraparib	–	–	–	2 (0.33%)	6 (0.49%)	8 (0.35%)	53.56 ± 12.23
	VEGFRi + PD-1i	Bevacizumab + Carrilizumab、Bevacizumab + tislelizumab、Bevacizumab + Sintilimab、Apatinib + Sintilimab	–	–	–	2 (0.33%)	2 (0.16%)	4 (0.17%)	60.89 ± 6.21
	EGFRi + PD-1i	Anlotinib + Tirellizumab	–	–	–	–	1 (0.08%)	1 (0.04%)	47.38 ± 18.70
Total		80	190	268	580	1190	2308	55.61 ± 11.13	

Note PARPi: Poly ADPRibose Polymerase inhibtor, VEGFRi: Vascular Endothelial Growth Factor Receptor inhibitor, EGFRi: Epidermal Growth Factor Receptor inhibitor, HER2i: Human Epidermal Growth Factor Receptor 2 inhabitor, PD-1i: Programmed Death-l inhibitor, mTORi: Mammalian Target Of Rapamycin inhibitor, ALK、MET、ROS1i: Multiple Tyrosine Kinases inhibitor, PDGFRi: Platelet-Derived Growth Factor Receptor inhibitor, MEKi: Mitogen-activated Extracellular Signal-regulated Kinase inhibitor, TKi: Tyrosine Kinase inhibitor.

Table 3
Main therapeutic drugs of the patients (n = 2308).

Classification	Therapeutic drugs	2017	2018	2019	2020	2021	Tatol	Mean age
VEGFRi	Bevacizumab	19 (23.75%)	55 (28.95%)	66 (24.72%)	168 (28.96%)	358 (30.08%)	666 (28.86%)	56.60 ± 10.54
VEGFR i + PD-1i	Bevacizumab + Camrelizumab	–	–	–	–	1 (0.08%)	1 (0.04%)	72.00 ± 0.00
VEGFRi + PD-1i	Bevacizumab + Tislelizumab	–	–	–	–	1 (0.08%)	1 (0.04%)	57.20 ± 0.00
VEGFRi + PD-1i	Bevacizumab + Sintilima	–	–	–	1 (0.17%)	–	1 (0.04%)	59.87 ± 0.00
PARPi	Olaparib	–	–	–	197 (33.96%)	398 (33.44%)	595 (25.78%)	57.77 ± 9.27
VEGFRi + PARPi	Bevacizumab + Olaparib	–	–	–	1 (0.17%)	4 (0.33%)	5 (0.22%)	53.60 ± 6.12
VEGFRi + PARPi	Renvastinib + Olaparib	–	–	–	–	1 (0.08%)	1 (0.04%)	51.00 ± 0.00
HER2i	Trastuzumab	–	51 (26.84%)	119 (44.57%)	82 (14.14%)	85 (7.14%)	337 (14.60%)	52.35 ± 9.83
VEGFRi	Apatinib	21 (26.25%)	66 (34.73%)	52 (19.48%)	30 (5.17%)	44 (3.69%)	213 (9.23%)	56.05 ± 7.89
VEGFRi + PARPi	Apatinib + Olaparib	–	–	–	1 (0.17%)	–	1 (0.04%)	54.50 ± 0.00
VEGFRi + PARPi	Apatinib + Niraparib	–	–	–	–	1 (0.08%)	1 (0.04%)	60.00 ± 0.00
VEGFRi + PD-1i	Apatinib + Sintilima	–	–	–	1 (0.17%)	–	1 (0.04%)	45.00 ± 0.00
EGFRi	Anlotinib	–	–	12 (4.49%)	46 (7.93%)	90 (7.56%)	148 (6.41%)	56.07 ± 11.16
EGFRi + PARPi	Anlotinib + Olaparib	–	–	–	–	6 (0.50%)	6 (0.26%)	58.50 ± 6.32
EGFRi + PARPi	Anlotinib + Niraparib	–	–	–	–	3 (0.25%)	3 (0.13%)	65.67 ± 1.25
EGFRi + PD-1i	Anlotinib + Tirezumab	–	–	–	–	1 (0.08%)	1 (0.04%)	42.00 ± 0.00
PARPi	Niraparib	–	–	–	–	103 (8.65%)	103 (4.46%)	56.54 ± 8.82
EGFRi	Nimotuzumab	–	10 (5.26%)	15 (5.62%)	26 (4.48%)	14 (1.18%)	65 (2.82%)	53.75 ± 10.98
PD-1i	Sintilimab	40 (50.00%)	–	–	7 (1.20%)	27 (2.27%)	74 (3.21%)	53.75 ± 10.80
HER2i	Pertuzumab	–	–	–	3 (0.51%)	5 (0.42%)	8 (0.35%)	55.00 ± 4.79
HER2i	Pertuzumab + Trastuzumab	–	–	–	7 (1.20%)	10 (0.84%)	17 (0.74%)	53.56 ± 12.23
EGFRi	Gefitinib	–	3 (1.59%)	–	6 (1.03%)	4 (0.33%)	13 (0.56%)	64.08 ± 13.66
EGFRi	Osimertinib	–	–	1 (0.37%)	–	–	1 (0.04%)	61.00 ± 0.00
TKi	Dasatinib	–	–	1 (0.37%)	–	–	1 (0.04%)	56.00 ± 0.00
PDGFRi	Imatinib	–	–	1 (0.37%)	–	1 (0.08%)	2 (0.09%)	51.50 ± 12.50
PD-1i	Camrelizumab	–	–	–	2 (0.34%)	12 (1.01%)	14 (0.61%)	45.64 ± 12.01
mTORi	Everolimus	–	–	–	2 (0.34%)	6 (0.50%)	8 (0.35%)	67.25 ± 9.65
ALK、C-MET、ROS1i	Crizotinib	–	–	–	–	2 (0.17%)	2 (0.09%)	48.00 ± 18.00
VEGFRi	Renvastinib	–	–	–	–	3 (0.25%)	3 (0.13%)	60.33 ± 0.47
MEKi	Trametinib	–	–	–	–	1 (0.08%)	1 (0.04%)	42.00 ± 0.00
PD-1i	Triplimab	–	–	–	–	1 (0.08%)	1 (0.04%)	45.00 ± 0.00
PD-1i	Tirellizumab	–	–	–	–	7 (0.58%)	7 (0.30%)	47.57 ± 9.50
HER2i	Initumab	–	–	–	–	1 (0.08%)	1 (0.04%)	59.00 ± 0.00
Tatol		80	190	268	580	1190	2308	55.61 ± 11.13

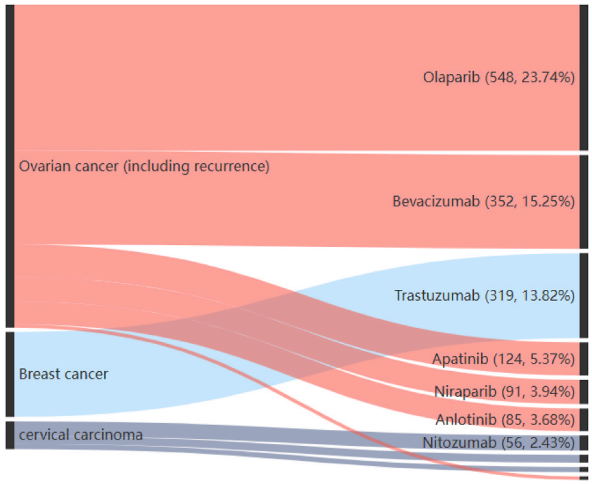

Fig. 1. Top ten novel antineoplastic targeted drugs detected in the patients.

Table 4
Cost of therapeutic drugs use per person each quarter from 2017 to 2020.

Treatment methods	Therapeutic drugs	2017	2018	2019	2020	2021	Amount (RMB)	Number of patients	Per capita (RMB)
Monotherapy	Bevacizumab	5058.24	8907.18	8784.32	6926.05	6908.6	36584.39	666	7570.77
	Bevacizumab	–	8811.83	7820.00	5569.51	5833.13	28034.47	337	7018.69
	Nituzumab	–	6800	7706.67	5850.38	6970.00	27327.05	65	6666.00
	Sintilimab	–	–	–	8122.85	6949.56	15072.41	74	3304.03
	Pertuzumab	–	–	–	4955.00	4955.00	9910.00	8	4955.00
	Initumab	–	–	–	–	1180.00	1180.00	1	1180.00
	Initumab	–	–	–	29700.00	5740.00	35440.00	14	9162.86
	Triplimab	–	–	–	–	2100.97	2100.97	1	2100.97
	Tislelizumab	–	–	–	–	6228.57	6228.57	7	6228.57
	Olaparib	–	–	–	17099.02	12117.78	29216.80	595	13767.03
	Niraparib	–	–	–	–	11133.98	11133.98	103	11133.98
	Apatinib	17664.21	2630.62	2503.16	2545.40	2454.21	27797.60	213	2751.76
	Anlotinib	–	–	4152.83	6384.58	2964.22	13501.63	148	4123.68
	Lapatinib	169.95	177.40	133.32	–	–	480.67	6	80.11
	Gefitinib	–	8667.00	–	1112.23	711.10	10490.33	13	1621.06
	Osimertinib	–	–	7650.00	–	–	7650.00	1	7650.00
	Dasatinib	–	–	1686.00	–	39.08	1725.08	1	862.54
	Imatinib	–	–	1686.00	–	39.08	1725.08	2	862.54
	Crizotinib	–	–	–	–	6244.60	6244.60	2	6244.60
	Renvastinib	–	–	–	–	4320.00	4320.00	3	4320.00
	Trametinib	–	–	–	–	11085.00	11085.00	1	11085.00
	Everolimus	–	–	–	4244.10	5008.80	9252.90	8	4817.73
Combined	Anlotinib + Olaparib	–	–	–	–	14373.61	14373.61	6	14373.61
	Anlotinib + Niraparib	–	–	–	–	13012.37	13012.37	3	13012.37
	Anlotinib + Tislelizumab	–	–	–	–	4666.88	4666.88	1	4666.88
	Apatinib + Olaparib	–	–	–	10614.00	–	10614.00	1	10614.00
	Apatinib + Sintilimab	–	–	–	5916.00	–	5916.00	1	9450.00
	Apatinib + Niraparib	–	–	–	–	9450.00	9450.00	1	9450.00
	Olaparib + Bevacizumab	–	–	–	29428.00	22749.00	52177.00	5	24084.80
	Olaparib + Renvastinib	–	–	–	–	8952.00	8952.00	1	8952.00
	Pertuzumab + Trastuzumab	–	–	–	11948.57	10568.05	22516.62	17	11137.24
	Bevacizumab + Sintilimab	–	–	–	20372.00	–	20372.00	1	20372.00
	Bevacizumab + Camrelizumab	–	–	–	–	5928.00	5928.00	1	5928.00
	Bevacizumab + Tislelizumab	–	–	–	–	9152.00	9152.00	1	9152.00
Tatol		22892.4	35994.03	42122.3	170787.69	201835.59	473632.01	2308	8630.80

4. Discussion

There is relatively little research on the application of novel anti-tumor drugs in gynecological cancer patients in China. Our study discusses the demographic characteristics of patients, the types of drugs used by patients, the chart and cost of drug diagnosis, and analyzes whether the selection of treatment plans and the use of drugs are reasonable.

4.1. Demography characteristics

According to our statistical findings, 37.86% of patients taking novel anti-tumor medications were aged of 51-60. People over 60-year-old accounted for 32.30% of all patients. The median age was 55.61-year-old. It is clear that the incidence of gynecological cancer patients rises with age. Gynecological reproductive cancers, such as cervical cancer, ovarian cancer, and endometrial cancer, are more common. These three major gynecological tumors are known as the three major gynecological tumors. This research findings are largely compatible with international literature research. According to Ama Buskwofie et al., the global average diagnostic age of cervical cancer is 53-year-old and the global average age is 59-year-old [7]. In China, the median age of onset for cervical cancer patients is 51-year-old, however it mostly occurs in two age groups, with the highest incidence occurring between 40 and 50 years old, and a peak occurring between 60 and 70 years old. It is uncommon before the age of 20, which is both similar and dissimilar to our findings [8]. China's Ovarian Cancer Guidelines [9] stated in 2022 that epithelial ovarian cancer, which represents for 80% of ovarian cancer incidence, is typically observed in postmenopausal women, which nearly overlaps the age category of this study. According to related data, malignant tumors above the age of 50-year-old account for the greatest number of deaths, accounting for 91.57%, with the middle-aged and elderly constituting the high-risk demographic for tumors [10]. The main causes of the high incidence of cancer in this age group and the high use of novel anti-tumor drugs in China are the rising in the elderly population, the gradual deterioration of middle-aged and elderly people's physical abilities, the gradual aging and decline of various organs, and the decline in resistance and immunity.

Guangzhou has the highest patient percentage among the five statistical cities. The combined detection of tumor markers can improve the sensitivity and the accuracy of gynecological malignant tumor diagnosis, helping guide clinical treatment, and efficient screening methods play a key role in the prevention of malignant tumors, which may be related to the efficient screening method in the hospital in Guangzhou, according to Ou Qianting et al.'s analysis of the epidemiological characteristics of 1262 deaths of malignant tumor patients between 2013 and 2018 [11,12].

4.2. Drug categories

VEGFRi variants, such as Bevacizumab and Apatinib, were the most often used novel anti-tumor medications among the nine main Chinese cities, and they increased year by year over the past five years, accounting for 38.08% of the entire study population (Table 2). The placental growth factor, VEGF-A, VEGF-B, VEGFR-C, and VEGFR-D are all members of the VEGF family. Many cancer tissues, such as liver, lung, colon, ovarian, breast, and others, have an overexpression of VEGF [13]. Drugs that targeted VEGF don't have a lot of selectivity. By reducing the expression of vasoactive factors, they primarily prevent tumor angiogenesis, cut off the tumor's supply, and prevent tumor development, recurrence, and metastasis. Representative medications like Bevacizumab, a humanized IgG1 type monoclonal antibody, are frequently used to treat tumor types including colorectal cancer, non-small cell lung cancer, hepatocellular carcinoma, cervical cancer, and others.

Bevacizumab rated top among all new anti-tumor medication therapy protocols according to the subgroup analysis in Table 3, while Apatinib came in ninth. The widespread use of VEGFR inhibitors in gynecological reproductive cancers may be closely related to this. Bevacizumab can be widely used as the initial treatment, maintenance treatment, and post-recurrence treatment of epithelial ovarian cancer, one of the top three gynecological tumors, according to the 2023 NCCN ovarian cancer guidelines [14]. The 2023 NCCN cervical cancer guidelines also noted that Bevacizumab is used in the first-line treatment and second-line or maintenance treatment of metastatic, recurrent, and persistent cervical cancer [15]. The increased use of Bevacizumab may result from this.

PARPi, which includes medications like Olaparib and Niraparib, is the second most often utilized class of medication. Multiple studies have demonstrated that PARP maintenance therapy, which has emerged as a new modality of ovarian cancer treatment, can considerably increase the survival time of patients with newly diagnosed or platinum sensitive recurrent ovarian cancer [16]. 70% of ovarian cancer patients are in an advanced clinical stage when they seek medical attention, making it the most prevalent and deadly gynecological malignancy.For newly discovered ovarian cancer, platinum-based combination chemotherapy and tumor cell reduction surgery are the first lines of treatment. After initial therapy, the majority of patients can achieve clinical remission, however 70% of patients still experience relapses within 2–3 years, and the 5-year survival rate has been averaging around 40%. The discovery of PARPi in recent years has fundamentally altered how ovarian cancer is treated. The use of PARPi after achieving a complete response (CR) and partial response (PR) after initial treatment or platinum sensitive recurrence treatment can significantly extend the progression free survival (PFS) time of ovarian cancer patients, according to a number of high-level evidence-based medical studies. The way that ovarian cancer is treated has changed as a result of PARPi maintenance therapy [17].

Due to the rising incidence rate of ovarian cancer, the amount of PARPi was zero from 2017 to 2019, then considerably increased in 2020 and 2021. It may be related to that Olaparib and Niraparib are the first PARPi drugs for ovarian cancer to receive approval in China and the US. Third place went to the HER2i single medication regimen, which used Trastuzumab or Inistumab. Her2i combination scheme (Trastuzumab + Parstuzumab) in the multi-drug combination scheme did not reflect the amount in 2017–2019, gradually growing from 2017, reaching its high in 2019 (accounting for 44.40%), and gradually dropping from 2021. The sum started

to increase dramatically in 2020–2021, placing it first in the combination plan. Mohd et al. [18] reported that according to the Global 2020 report, Asia has the highest incidence rate, followed by Europe and North America, and the cancer with the highest incidence rate is breast cancer. It was reported [19] that the incidence rate of breast cancer is 47.8 cases per 100,000 people, indicating that the incidence rate of cancer is still high. In China, both in urban and rural areas, breast cancer ranks first in the female cancer incidence spectrum, and the top four in the female cancer death spectrum, which is also the most common type of cancer in general, second only to lung cancer [20]. According to He Siyi et al. [21], the incidence rate of female breast cancer in some Asian countries has also been shown an obvious upward trend in the last 30 years, with the growth rate being significantly higher than that in Europe and the United States, but there are still some differences between China and the United States and other countries. Among these, the average annual percentage change (AAPC) in the incidence rate of female breast cancer in China from 1988 to 2012 was 4.1% (95% CI: 3.0%-5.1%). This is consistent with the study's finding of a considerable increase in HER2i usage beyond 2020. Furthermore, in this paper, the average age of HER2i alone is 52.43 $\pm$ 9.75 years, and the average age of the population with HER2i combo regimen is 42.00 $\pm$ 9.75 years, indicating that the age of occurrence of HER2i positive breast cancer in China is relatively early. According to He'sliterature, the peak incidence rate of breast cancer in Asian women occurred in the younger age group. Breast cancer is most common in women aged of 60–64 in China, Japan, and South Korea. The maximum age group was 55 $\pm$ 59 years old and 50 $\pm$ 54 years old. The average age of breast cancer in this trial was younger, which was likely due to HER2i primary indication being HER2i positive breast cancer, which did not represent all breast cancer.

Interestingly, we can see that the dosage of new anti-tumor drugs has increased in recent years, which can be attributed to the rapid development of clinical practise in tumor treatment and the continuous innovation of new technologies, as well as the shift towards precise and personalised treatment in tumor medicine.

4.3. Per capita cost of medication

In terms of time, the proportion of expenses spent from 2017 to 2021 would rise year by year, rising from 2.23% in 2017 to 52.29% in 2021. The difference between the two is statistically significant ($P < 0.001$). Bevacizumab, Olapari, Trastuzumab, Apatinib, and Nituzumab are the top five new anti-tumor drugs with the highest total single drug amount, reflecting that VEGFRi and PARPi have a wide range of indications in current clinical trials of gynaecological tumors and are marketed early, so the growth rate is relatively high. Olaparib, Niraparib, Trimetinib, Karelizumab, and Oxetinib have the highest per capita quarterly expenses for single medication regimens, which may be connected to the fact that these novel anti-tumor drugs have not yet entered the Chinese medical insurance catalogue. In the joint plan, the top five quarterly expenses per capita were Olaparib + Bevacizumab, Bevacizumab + Cindilimab, Arotinib + Olaparib, Arotinib + Niraparib, and Apatinib + Olaparib. Similarly, these drug plans include more innovative anti-tumor treatments not covered by medical insurance. The entire quarterly cost per capita is 8630.80 RMB, and the overall burden of patients utilising novel anti-tumor medications is relatively heavy. At the moment, the country is also pursuing steps, such as national bulk procurement and medical insurance talks, to drastically cut treatment costs, which will be a huge step towards reducing the burden on patients.

5. Conclusion

From January 2017 to December 2021, we analyzed gynaecological outpatient and inpatient prescriptions for anti-tumor medications. In the past five years, the greatest number of novel anti-tumor drugs were prescribed to patients aged of 51–60, and the incidence rate increased as age increased. This is due to the growing geriatric population in China, the gradual decline of middle-aged and elderly people's physical abilities, the gradual ageing and decline of various organs, and the decline of resistance and immunity. VEGFRi was the most frequently used new anti-tumor drug in China nine largest cities, and its usage has increased annually over the past five years (2017–2021). Bevacizumab dosage ranked first, followed by PARPi. The proportion of expenses incurred between 2017 and 2021 has increased annually. Guangzhou had the greatest proportion of patients, which may be attributable to its effective screening procedures. Second, in the combined application scheme, HER2i had the highest proportion of combination, which may be related to the highest breast cancer incidence rate in China. In addition, the per capita quarterly cost analysis reveals that the use of new oncology drugs places a relatively heavy burden on patients, and the country is presently taking steps to reduce residents' medication costs. Future research may concentrate on how novel antitumor drugs can minimize the economic burden and maximize the benefits of patient treatment for patients with gynaecological cancer.

Ethics statement

Informed consent was not required for this study because this study did not infringe on the privacy of patients, the ethics committee agreed to waive the application for informed consent. Thus, we did not apply for the approval from the Hospital Medical Ethics Committee.

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Limitations

Our study has some limitations. First, the majority of the study population was from economically developed regions in China. The prescription patterns in some underdeveloped areas may be different due to discrepancies in access to medical and economic factors. Second, the study counted the prescriptions of patients diagnosed with new anti-tumor drugs, but the chemotherapy or surgical outcomes of these patients before and after using the new anti-tumor drugs were not included in the discussion. Third, due to the lack of information on disease severity, such as staging, our data does not support subgroup analysis to explore prescription differences among patients with different disease severity levels.

Data availability statement

The data associated with our study has not been deposited into a publicly available repository, and the data has been included and referenced in the article.

CRediT authorship contribution statement

Changyan Li: Writing – original draft, Methodology. **Jing Jin:** Software, Data curation. **Jing Tang:** Writing – review & editing, Resources, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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