



Awareness, understanding, attitude, and barriers toward prescribing modern cancer immunotherapies in the Arabian Gulf countries

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Abstract

Introduction: The use of modern immunotherapy has been evolving over the past few years, and various new agents have been developed for new indications at multiple primary sites in oncology. It is important for physicians who are involved in cancer care to be aware and updated about new therapeutic agents and their indications, potential benefits, and side effects.

Patients and Methods: From October to November 2017, we conducted a survey on the awareness, understanding, attitude, and barriers associated with prescribing modern cancer immunotherapies among physicians in the Arabian Gulf countries. The study included practicing physicians who delivered chemotherapy; trainees were not eligible. A total of 460 physicians were contacted and invited to complete an online survey, of which approximately 74.8% did not respond, and 4 (3.4%) were excluded because they had not recently treated patients with cancer. 112 (24.3%) physicians completed the survey (completion rate = 25.2%). An online electronic survey questionnaire was developed via Planet Surveys. The survey was designed with multidisciplinary inputs of the study investigators practicing in the Arabian Gulf countries, piloted, and subsequently revised on the basis of feedback from 10 additional oncologists. The final survey included 23 questions and took 8–10 minutes for completion.

Results: All respondents were aware of modern immunotherapies, but 62.5% reported having limited experience in implementing them, whereas 31.3% reported good experience. The overall physicians' attitudes toward modern immunotherapy were favorable, with a mean score of 7.4 (scale of 1–10, with 10 being extremely favorable). Efficacy, clear indications, and good safety profile were perceived as key potential benefits. Cost, lack of experience, and lack of access to specific testing were the major barriers.

Discussion and Conclusion: Patients were likely to be receptive to modern immunotherapy as a therapeutic option for cancer treatment. Long-term efficacy data, financial support programs, and educational activities for prescribers may increase the access to modern immunotherapy.

Keywords: Immunotherapy, Personalized medicine, Arab World, Middle east, Mutation

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Introduction

Immunotherapy has been under evaluation for more than a century, but only recently has it entered a renaissance phase with the approval of multiple agents for the treatment of cancer ⁽¹⁾. Cancer immunotherapy encompasses a variety of treatment approaches, including passive administration of tumor-specific monoclonal antibodies and other immune system components as well as adoptive transfer of ex vivo modified T cells, active immunization to elicit or augment specific T-cell-mediated immune responses against tumor cells, and administration of immune modulatory agents for nonspecific enhancement of immune responsiveness ^(2,3). Modern immunotherapies include but are not limited to checkpoint inhibitors that target the programmed cell death 1 (PD-1) or PD ligand 1 and monoclonal antibodies directed against cytotoxic T-lymphocyte antigen 4 have demonstrated improved overall survival in patients with metastatic cancers from multiple primary sites ⁽⁴⁻⁸⁾.

The field of cancer immunotherapy has rapidly evolved over the last few years. The first approval for using modern immunotherapy agents (excluding PROVENGE® for metastatic castrate-resistant prostate cancer) was for ipilimumab for treating metastatic advanced melanoma in March 2011 ⁽⁹⁾. Until November 2017, 36 indications have been approved by the United States Food and Drug Administration (FDA) for modern immunotherapeutic agents at different disease sites and with different mechanisms of action. In 2017, we have witnessed the highest number of approvals per year for modern immunotherapies in FDA history, with 16 new indications (44.4% of all modern immunotherapies approved by the FDA since 2011 were in 2017) ⁽¹⁰⁾.

Physicians involved in cancer care are under tremendous pressure to be updated about novel treatments approaches, including immunotherapies. It includes understanding of the mechanisms of action of these novel agents; their potential benefits, indications, and side effects; and management of unusual side effects which differ from those of usual chemotherapeutic agents' toxicity profiles. The Gulf Cooperation Council countries, which are also known as the Arabian Gulf countries, include Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates (UAE), and are rapidly growing both economically and demographically. The health care systems in the Arabian Gulf countries are ranked in the top 45 systems worldwide according to the most recent World Health Organization report in 2000 ⁽¹¹⁾. According to the GLOBOCAN 2012 report, there were 24,528 newly diagnosed cancer cases in the Arabian Gulf countries, and this number is expected to increase by 1.7 fold to reach 43,245 new cases by 2025 ⁽¹²⁾.

We conducted a survey of physicians in direct contact with cancer patients in the Arabian Gulf countries. The objectives of the survey were to assess the awareness, understanding, attitudes, and barriers associated with prescribing modern cancer immunotherapies in these countries, and to identify priorities for educational needs to enhance patient care.

Methods

Study population

The study population included any practicing physician who was prescribing chemotherapy; trainees were not eligible. The web-based survey was distributed using a modified snowball methodology. As a means of identifying potential participants, we contacted oncologists in Saudi Arabia, the UAE, Oman, Bahrain, and Kuwait. The contact was preferentially directed to established national associations of medical oncologists; if this was not possible, we approached one to two personal contact per country to invite participation and distribute the survey via an informal national network. This study was approved by the Research Ethics Board of the University of Sharjah.

Survey design and distribution

An online electronic survey questionnaire was developed via Planet Surveys (Appendix 1) to capture the following information: awareness, understanding, attitude, and barriers associated with prescribing modern cancer immunotherapies. The survey was designed with multidisciplinary inputs from the study investigators practicing in the Arabian Gulf countries. Then, it was piloted and subsequently revised based on the feedback received from 10 additional oncologists. The final survey included 23 questions and required 8–10 min for completion; the instrument can be seen in Appendix 1.

Two primary methods were used to distribute this survey. The primary investigator (HOA) contacted individuals and regional oncology associations to create a broad distribution network. The regional contacts, which were either associations or individuals, were provided an electronic link to the survey to be distributed to their regional members/networks. The five distributing partners were asked to provide the team with an estimated number of survey recipients to ascertain the national response rate for the survey. The survey was distributed in October 2017. A reminder email was sent in November 2017.

Results

Participants

From October to November 2017, 460 physicians were contacted and invited to complete the online

Speciality	Medical oncologist and hematologist	Medical oncologist only	Hematologist only	Clinical oncologist (provides both chemotherapy and radiotherapy)
No. of participants	23	48	29	12
Saudi Arabia	13	32	17	5
UAE	3	4	4	4
Kuwait	3	5	3	2
Bahrain	2	4	3	1
Oman	2	3	2	0

Table 1. Number of participants according to their specialties and countries. Participants were practicing in various subspecialties of oncology (solid tumors and malignant hematology).

survey. Among all physicians contacted, approximately 74.8% did not respond and four (3.4%) did not meet the screening criteria primarily because they had not recently been active in treating patients with cancer. In total, 112 (24.3%) physicians who responded to the invitation to participate, met the screening criteria, and completed the survey (completion rate = 25.2%) were included in the study (Table 1). Overall, 85 (75.8%) of the completers were practicing either medical oncology or hematology or both, and 26 (23.2%) were practicing clinical oncology (prescribing chemotherapy and radiotherapy). The numbers of respondents according to their countries and specialties are summarized in Table 1. Respondents reported practicing in various subspecialties of oncology and hematology (Figure 1).

Awareness, understanding, and attitudes associated with prescribing modern cancer immunotherapies

The majority (62.5%) of the respondents reported having limited experience in prescribing modern immunotherapy (<30 patients treated with modern immunotherapy), whereas 31.3% reported having

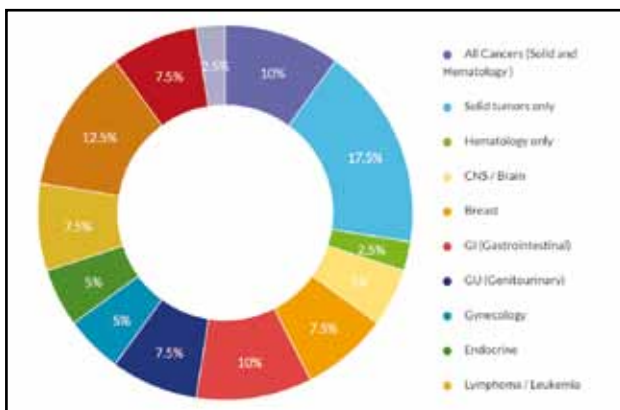


Figure 1. Respondents who reported subspecialties of oncology and hematology.

sufficient experience (≥ 30 patients treated with modern immunotherapy). Furthermore, 6.3% of respondents were aware of immunotherapy but had no experience in prescribing them. None of the respondents reported of lack of awareness of immunotherapy or its indications (Figure 2).

In assessing the overall attitude toward cancer immunotherapy on a scale of 1–10, where 1 is not at all

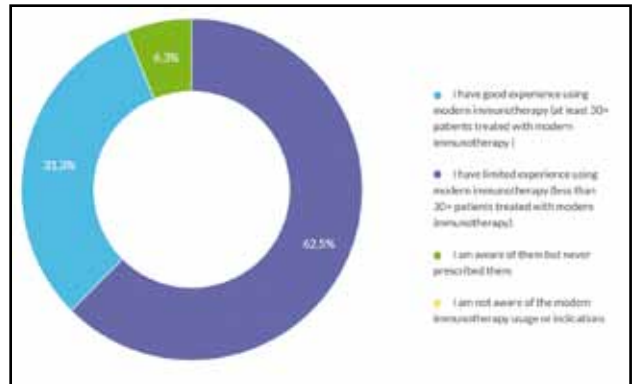


Figure 2. Awareness and understanding of modern cancer immunotherapies.

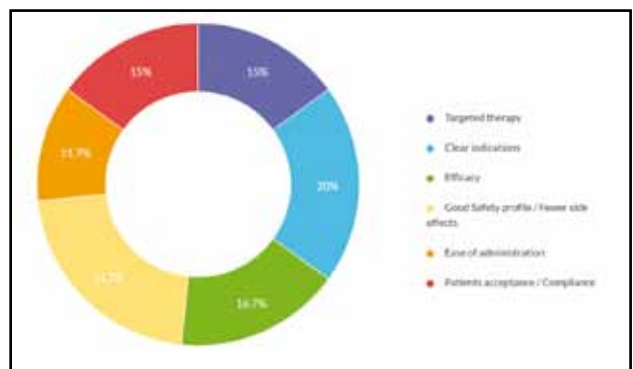


Figure 3. Benefits of modern immunotherapy during the respondents' clinical practice.

favorable and 10 is extremely favorable, the mean score was 7.4, which indicates a favorable attitude toward cancer immunotherapy.

Usage and barriers in prescribing cancer immunotherapy

The responses concerning the potential benefits of using modern immunotherapy showed that 21.7% of the respondents cited a good safety profile for immunotherapy, 20% cited clear indications for usage, 16.7% cited evidence of efficacy, 15% cited targeted therapy, and 15% cited patient acceptance and compliance (Figure 3).

In addressing the barriers associated with prescribing immunotherapy in their own clinical practice, 37.2% of the respondents reported cost and reimbursement issues as the top barrier, 20.9% reported lack of experience

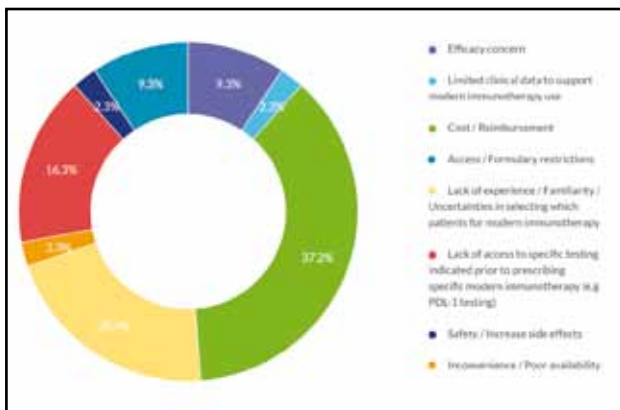


Figure 4. Barriers in using cancer immunotherapy.

and uncertainties in selecting suitable patients for modern immunotherapy, 16.3% reported lack of access to specific testing prior to prescribing a specific modern immunotherapy (e.g., PD-1 testing), and 9.3% reported efficacy concerns (Figure 4). A total of 87% of the respondents agreed that having a patient financial support program would increase the access to modern immunotherapy for patients.

Need for educational information

A total of 64.7% of the respondents reported being comfortable in managing the side effects of modern immunotherapy, 17.6% reported not feeling comfortable, and 17.6% reported neutral responses (Figure 6). All respondents who were not comfortable or were neutral in their response regarding the side effects were directed to answer a question on the importance of conducting educational activities for modern immunotherapy before starting to prescribe it (Figure 7). Among the respondents who were initially not comfortable with dealing with the side effects, 81.3% indicated their interest in participating

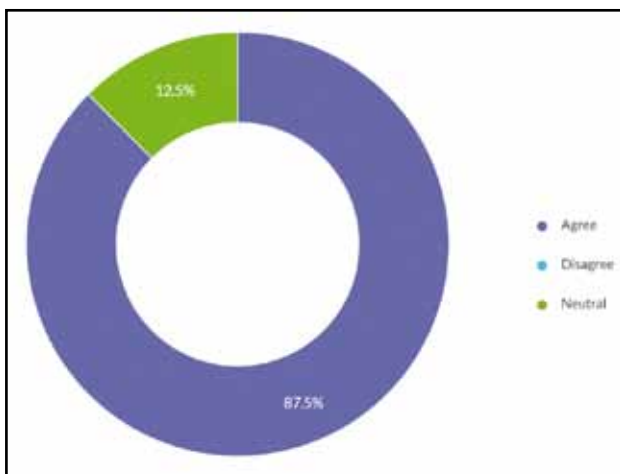


Figure 5. Having a patient financial support program will increase the access to modern immunotherapy for patients with limited insurance/no insurance in my practice.

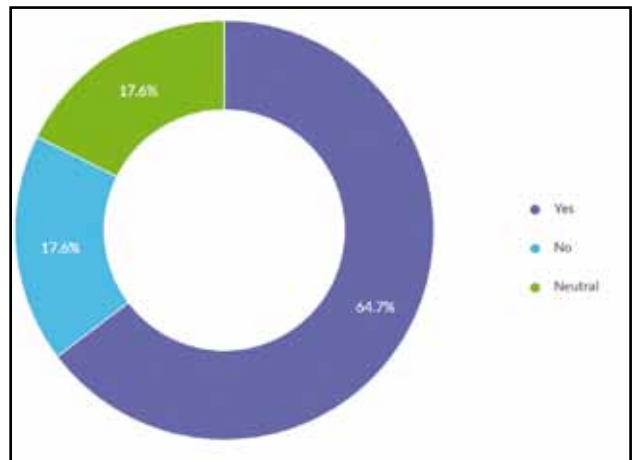


Figure 6. I am very comfortable in dealing with the side effects associated with modern immunotherapy.

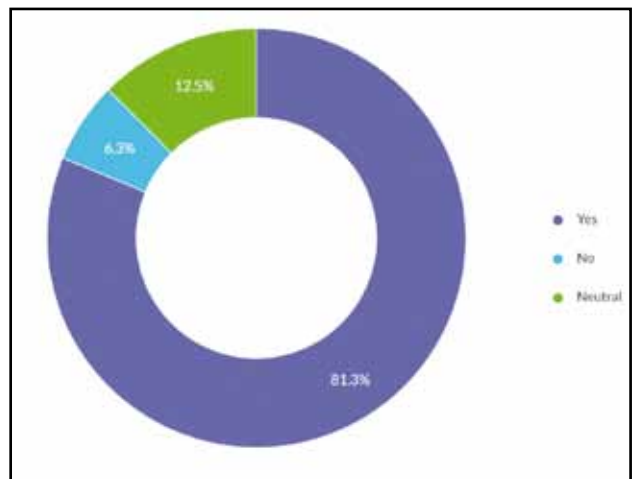


Figure 7. I would like to have more educational activities for modern immunotherapy before I start prescribing it.

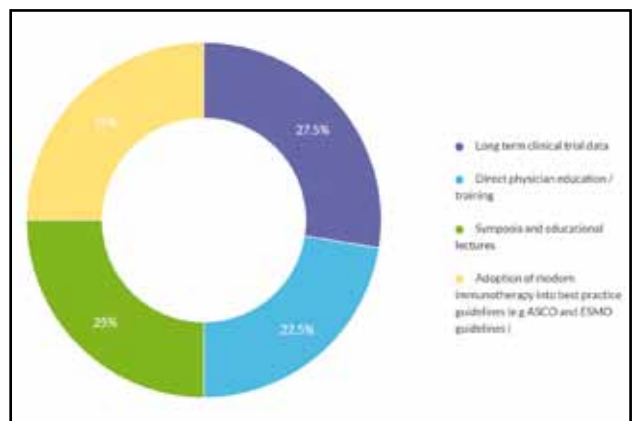


Figure 8. Types of information required to increase the knowledge/belief in cancer modern immunotherapy.

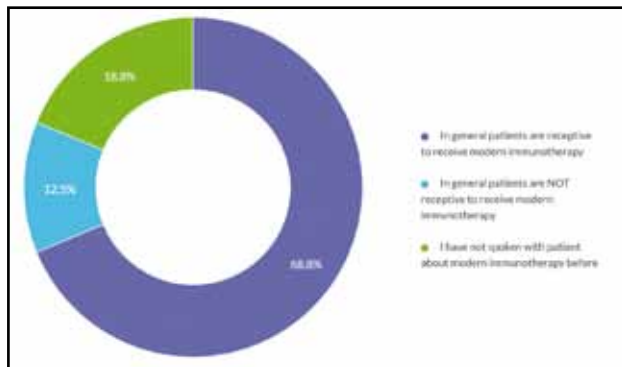


Figure 9. How would you rate your patients' receptivity to cancer modern immunotherapy as a therapeutic option?

in educational activities prior to prescribing modern immunotherapy (Figure 8).

Finally, 68.8% of the respondents reported that it was important that patients be receptive to cancer modern immunotherapy as a therapeutic option (Figure 9).

Discussion

Modern immunotherapy has evolved rapidly over the past few years. The fast pace of approvals for various indications, including the first FDA approval for pembrolizumab for solid tumors harboring microsatellite instability (MSI) status rather than organ-specific approval⁽¹³⁾, has revolutionized the way we evaluate and treat cancer. Multiple immunotherapeutic agents have been used various indications, such as interleukin-1 for renal cell carcinoma¹⁴, interferon alpha for malignant melanoma¹⁵, and sipuleucel-T for advanced castrate-resistant prostate cancer¹⁶. However, the use of these agents has been limited by their efficacy^(14–16).

A better understanding of the unique interaction between the immune system and cancer cells has led to the development and approval of multiple immunotherapeutic agents for multiple primary cancers^(4–8). Currently, numerous ongoing clinical trials have been assessing the existing as well as novel immunotherapeutic agents for various indications⁽¹⁷⁾. The abundance of immunotherapeutic agents and their indications, complicated by nonstandardized testing for PDL-1 and MSI, have also created some scientific and clinical confusion regarding the optimal use of these agents and management of their unique and complex side effects. A limited number of studies have assessed the awareness, understanding, attitudes, and barriers associated with prescribing modern immunotherapies among oncologists⁽²⁾.

The present study is the first to evaluate these concepts among oncologists from the Arabian Gulf

countries. The response rate was low (25.2%), and was close to that in other similar health care surveys (2). A total of 59.8% of the respondents were from Saudi Arabia, which is consistent with the largest number of oncologists in the largest country among the Arabian Gulf countries. Additionally, 62.5% of the respondents reported having limited experience in using modern immunotherapy. We used an arbitrary cutoff of 30 treated patients as an indication of a reasonable level of experience in using immunotherapy, a definition that was agreed upon by the study coauthors. Good experiences in using modern immunotherapy (>30 patients under their care received chemotherapy) was reported by 31.3% of the respondents, awareness of immunotherapeutic drugs but no experience in prescribing them by 6.3%, and limited experience by 62.5% of the oncologists, which was high compared with 31.3% who reported having good experience, considering that the first modern immunotherapy agent was approved in 2011 by the FDA; however, it is important to understand that approval and availability of drugs in the Arabian Gulf countries are delayed than those in the U.S. by months to years. Additionally, each gulf country has its own regulatory authority, and the approval process varies based on the mechanism and timing of approval among the Arabian Gulf countries.

The overall attitude toward cancer immunotherapy was very positive, with a mean score of 7.4 (scale, 1–10). This result was possibly driven by the good clinical experience in using these agents, but may be biased due to multiple approvals for various immunotherapeutic agents with significant media attention just prior to the survey as 62.5% of the respondents had limited experience in using these agents.

There were a variety of reasons given by the respondents regarding what encouraged them to prescribe immunotherapy. The respondents were allowed to choose as many options as possible for this question, and 89% selected ≥ 3 reasons out of the 6 listed (Appendix 1), which indicated that there were many encouraging reasons to prescribe modern immunotherapy.

There were also multiple barriers to the use of immunotherapy in the respondents' clinical practice, with cost and reimbursement issues (37.2%) being the top barriers (Appendix 1). Of the 8 barriers listed, ≥ 4 were selected by 78% of the respondents. This finding highlights the current scientific, educational, and financial barriers that persist and need to be addressed to achieve proper utilization of immunotherapy. 87% of the respondents agreed that access to a patient financial support program would increase the usage of modern immunotherapy for patients, which may lead to better patient care and outcomes.

In addressing the information needed to increase the knowledge of, confidence in, and utilization of modern immunotherapy, the respondents identified long-term clinical trial data, adoption of modern immunotherapy into the best practice guidelines (e.g., the American Society of Clinical Oncology and European Society of Medical Oncology guidelines), symposia, and educational lectures as the top priorities that would enhance the respondents' knowledge, confidence, and experience in prescribing modern immunotherapy. Future research should evaluate the best methods of imparting knowledge regarding the prescription of newer agents and medications and managing their side effects.

Patients are likely to be receptive to modern cancer immunotherapy as a therapeutic option according to 68.8% of the respondents, which may be driven by significant media and public attention given to the latest breakthroughs in the development of immunotherapies and by FDA approvals for various immunotherapeutic agents.

Conclusion

There was a high level of awareness and an overall positive attitude toward modern cancer immunotherapy among oncologists in the Arabian Gulf countries, but there was a limited experience in prescribing cancer immunotherapeutic agents. Efficacy, clear indications, and good safety profile were perceived as key potential benefits, whereas cost, lack of experience, and lack of access to specific testing prior to prescription were the major barriers. Most respondents believed that patients were likely to be receptive to immunotherapy as a therapeutic option. Long-term efficacy data, financial support programs, and educational activities for prescribers may increase the access to modern immunotherapy.

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Appendix 1 – Survey Questionnaire

1. Do you agree to participate in this study? * Yes/No
2. Are you actively involved in direct cancer care including prescription of chemotherapy? Yes/No
3. Have you completed your training and you are fully licensed to practice and work independently (Residents and fellows are not eligible to participate)? Yes/No
4. Do you provide? Chemotherapy | Radiation therapy | Both Chemotherapy and Radiation therapy
5. What best describes you? Medical oncologist | Radiation oncologist | Clinical oncologists (Provide both Chemotherapy and Radiation therapy) | Hematologists | Gynecologist | Internal medicine physician practicing in oncology | Other
6. Which country are you mainly practicing in? (if you are practicing in more than one, then choose the one with most time practice being held at): Saudi Arabia | UAE | Oman | Kuwait | Bahrain
7. How many years since you completed you training? Less than 5 years | 5– 10 years | 11–15 years | More than 20 years
8. Do you work in: Public health setting | Private health care setting | Both public and private
9. Are you practicing in a rural or urban location? Rural defined as: two hours away from a tertiary cancer center and population of less than 50,000 | Urban | Rural
10. Which cancer do you treat? All cancers | Brain | Breast | Lung | Head and neck | GI GU (Genitourinary) | Gynecology | Endocrine | Lymphoma / Leukemia | Sarcoma | Skin / Cutaneous | Others
11. I mainly treat: Adults | Paediatric | Both adults and pediatrics
12. In average month, I participate in the multidisciplinary tumor board for: 0 (We do not have access to multidisciplinary tumor board) | 1 | 2 | 3 | 4+
13. How many new cancer cases do you see pear year? (Average) : <100 | 100–200 | 201–300 | 301–400 | 401–500 | >500
14. What percentage of you patients will be prescribed any form of anticancer treatment (Chemotherapy, targeted therapy, hormonal, immunotherapy)? 0–20% | 21–40% | 41–60% | 61–80% | 81–100%
15. Which of the following best describes your awareness of modern cancer immunotherapies:
 - I have good experience using modern immunotherapy (at least 30+ patients treated with modern immunotherapy)
 - I have limited experience using modern immunotherapy (less than 30+ patients treated with modern immunotherapy)
- I am aware of them but never prescribed them
- I am not aware of the modern immunotherapy usage or indications
16. Please indicate your overall attitude toward cancer immunotherapy where 1 means not at all favorable and 7 means extremely favorable.” This is a general question to assess comfort level with prescribing, efficacy of immunotherapy and satisfaction with patients’ outcome: 1–2–3–4–5–6–7–8–9–10 (Negative 1–3, Neutral 4–6, Positive 7–10)
17. The benefit of modern immunotherapy in my practice is (choose as many as needed): Targeted therapy | Clear indications | Efficacy | Good Safety profile / Fewer side effects | Ease of administration | Patients acceptance / Compliance
18. The limitation of modern immunotherapy in my practice (choose as many as needed)? Efficacy concern | Limited clinical data to support modern immunotherapy use | Cost / Reimbursement | Access / Formulary restrictions | Lack of experience / Familiarity / Uncertainties in selecting which patients for modern immunotherapy | Lack of access to specific testing indicated prior to prescribing specific modern immunotherapy (e.g PDL–1 testing) | Safety / Increase side effects | Inconvenience / Poor availability
19. Having patients’ financial support program will increase access to modern immunotherapy for patient with limited insurance / no insurance in my practice: Agree | Disagree | Neutral
20. I am very comfortable in dealing with side effects from modern immunotherapy: Yes | No | Neutral
21. I would like to have more modern immunotherapy educational activities before I start prescribing modern immunotherapy: Yes | No | Neutral
22. What types of information would be useful to increase your knowledge/belief in cancer modern immunotherapy?”
 - Long term clinical trial data
 - Direct physician education / training
 - Symposia and educational lectures
 - Adoption of modern immunotherapy into best practice guidelines (e.g ASCO and ESMO guidelines)
23. How would you rate your patients’ receptivity to cancer modern immunotherapy as a therapeutic option?”
 - In general patients are receptive to receive modern immunotherapy
 - In general patients are NOT receptive to receive modern immunotherapy
 - I am not sure
 - I have not spoken with patient about modern immunotherapy before