Research Article

Understanding immunotherapy and its management

Nadiminti Rajesh Kumar1* and Sajid Alvi2

1Research Scholar, Lotus Business School, Pune, India
2Director, DIMR, Pune, India

Received: 04 January, 2021
Accepted: 11 January, 2021
Published: 12 January, 2021

*Corresponding authors: Nadiminti Rajesh Kumar, Research Scholar, Lotus Business School, Pune, India, Tel: 8125245744; E-mail: rajeshkumarr32@gmail.com

Keywords: Immunotherapy; PD-1/PD-L1 mechanism; Tumor stroma role in PD-1/PD-L1; Immune resistance; Challenges and new approach; Combination immune therapy

https://www.peertechz.com

Abstract

A few tumours are exceptionally stubborn to oral chemotherapy. The endurance of tumours in a few cases is helped by checkpoint immunomodulation to keep up the unevenness between resistant reconnaissance and disease cell division. Checkpoint counteracting agent inhibitors, for example, against PD-1/PD-L1, are another class of inhibitors that capacity has tumour sti

<image>

...fling element using a balance of resistant cell/tumour cell communication. These checkpoint inhibitors are quickly turning into a profoundly encouraging malignancy helpful methodology that shows astounding antitumor reaction with restricted symptoms. As of late over four checkpoint inhibitors have been utilized for focusing on PD-1, PD-L1 and CTLA-4. Despite the immense achievement and viability of hostile to PD treatment reaction, it is restricted to explicit kind of malignant growths, which credits to the lacking and heterogeneous articulation of PD-1 in the tumour miniature condition. Thus, we audit the current extent of the PD-1/PD-L1 instrument function in tumour invulnerable avoidance and helpful result for malignant growth treatment.

Introduction

Immunotherapy is a kind of malignancy therapy that enables your safe framework to battle disease. The resistant framework enables your body to battle contaminations and different infections. It is comprised of white platelets and organs and tissues of the lymph framework. Immunotherapy is a sort of natural treatment. Natural treatment is a sort of therapy that utilizes substances produced using living life forms to treat malignant growth. Immunotherapy is a therapy that utilizes certain pieces of an individual resistant framework to battle illnesses, for example, malignancy this should be possible in two different ways. Stimulating your insusceptible framework to work more diligently or more brilliant to assault malignancy cells. Giving you insusceptible framework parts, for example, man-made framework proteins. In the most recent couple of decades, immunotherapy has become a significant piece of treating a few kinds of malignant growth. Fresher kinds of safe therapies are currently being contemplated, and they will affect how we treat malignant growth later on. Immunotherapy incorporates treatment that works in various manners. Some lift the body insusceptible framework in an overall way. Others help train the invulnerable framework to assault disease cells explicitly. The immune framework works better for certain kinds of disease than for other people. It’s utilized without anyone else for a portion of these tumours, yet for other people, it appears to work better when utilized with different kinds of treatment.

Current trends

There are a few developing patterns in immuno–oncology, including checkpoint inhibitors and Assenting T-Cell Treatment (ACT). Invulnerable checkpoint segments, for example, Cytotoxic T Lymphocyte antigen 4 (CTLA-4) and customized cell Passing 1 (PD-1) and its ligand (PD–L1) – are communicated on tumour–penetrating lymphocytes and numerous kinds of tumour cells, and they permit damaged cells to sidestep cytotoxic insusceptible reactions. Ipilimumab, a neutralizer focusing on CTLA-4 endorsed by the FDA for use in patients with melanoma, represses this cycle and encourages T–cell actuation against tumour cells. Antibodies focusing on PD-1 and PD-L1 are likewise being tried in stage III preliminaries.

Abbreviations

PL /PL-1: Programmed Cell / Programmed Cell-1; CTLA-4: Cytotoxic T Lymphocyte Associated Protein-4; ACT: Ascending T Cell Treatment; HPV: Human Papilloma Virus; ASCO: American Society of Clinical Oncology Journal; IMD: Different Immunomodulator; CAR –T-Cell: Chimeric Antigen Receptor-T cell; FDA: Food Drug Association

References

1. Kumar NR, Alvi S (2021) Understanding immunotherapy and its management. Int J Immunother Cancer Res 7(1): 001-007. DOI: https://dx.doi.org/10.17352/2455-8591.000030
against a few sorts of tumours. This year in Japan nivolumab turned into the first PD-1 inhibitor to accomplish administrative endorsement in melanoma. Promising outcomes have likewise been posted for the trial against PD-L1 counteracting agent MPDL3280A in melanoma, cellular breakdown in the lungs and bladder malignant growth. ACT, T cells enacted against tumour-explicit antigens are confined from the patient, extended ex vivo, and afterwards once again introduced into the patient. A stage I study introduced at the 2014 ASCO Annual Meeting tried Human Papillomavirus (HPV)- explicit T cells in patients with metastatic cervical malignant growth and created a few sturdy complete reactions.

**Literature review**

Cancer has clarified on the essential component of the insusceptible framework as it identifies with the disease has been expanding quickly which zeroed in on inspecting flow information and future bearings of exploration identified with tumour immunology and malignant growth immunotherapy, remembering meetings for inborn invulnerability, versatile resistance, helpful methodologies (dendritic cells, receptive T-cell treatment, against tumour antibodies, malignancy immunizations and safe checkpoint barricade), challenge to driving an enemy of tumor safe reaction, observing safe reactions and the eventual fate of immunotherapy clinical preliminary plan[1]. Immunotherapy has clarified the advancing function of immunotherapy medicines in India alongside the security and adequacy identified with kinds of immunotherapy medicines accessible [2]. Cancer Immunotherapy gave a short survey on the history prospects and difficulties ahead on malignant growth immunotherapy [3].

Cancer Immunotherapy examined the present and eventual fate of disease immunotherapy: A tumour miniature ecological point of view. Despite accomplishment in focusing on non-tumour cell segments, including insusceptible checkpoint blockage, focussing on a solitary invulnerable suppressive objective is insufficient in most of the patient with the malignant growth. Following obstructing or hindering of one invulnerable suppressive sign, the tumour will repay through another component to produce the opposition and decrease the proficiency of immunotherapy. The relationship between the heterogeneity of the tumour microenvironment and the immunotherapy reaction stays a critical test. Later on, immunotherapy might be needed to be customized for every patient with the disease as per the tumour microenvironment. The utilization of novel safe biomarkers [4] PD–L1 examined on the improvement of resistant checkpoint inhibitor has changed the therapy worldview for cutting edge diseases across numerous tumour type. Notwithstanding promising and now and then strong reactions in a subset of patients, most [5]. Immunotherapy has clarified the expanding utilization of different Immunomodulatory (IMD) agence for malignant growth treatments (eg: antibodies focusing on a resistant checkpoint, by explicit antibodies and illusory antigen receptor ((CAR)- T-cell). The advantage showed as far as long–haul reactions and infection control by endorsed IMD treatments and significance of adequately executing these treatment methodologies [6].

Cost of Immunotherapy in India: Its cost around 1 lakh to 1.3 Lakh for one treatment of Immunotherapy in India. In like clockwork, another treatment is needed to been given to the patient, if necessary. The expense of immunotherapy in India is just about 8–10 times lower than the expense of immunotherapy in western nations though there is no adjustment in the outcome and the cycle of treatment of both the parts. Cancer Immunotherapy isn’t advanced in India due to the reasoning and their perspectives on natively constructed sub–atomic medications and treatments. Along these lines, the absence of prevalence is one of the explanation that why immunotherapy isn’t advanced in India. Sometimes, it is seen that the immunotherapy sets aside a long–range of effort to regard malignancy when contrasted with other treatment techniques. Immunotherapy doesn’t take a shot by any stretch of the imagination. Cost is likewise an issue in a portion of the cases [7–15].

**Objectives of a research**

Immunotherapy is the most evolving treatment for cancer management.

a. To find out the institute-wise protocol
b. To find out how do doctors choose different immune therapy
c. To understand the different {PD-1 and PDL-1} Immunotherapy agents.
d. To understand the challenges faced by patients

**Research methodology**

Type of research: Exploratory and Descriptive

Research design: Qualitative and Quantitative

Sample size – 80

The present work includes mainly three steps

1. To prepare a questionnaire for doctors
2. Collect the responses from the Doctors
3. Analyse the results and to give the conclusion

**Hypothesis:** Every hospital has a cancer immunotherapy treatment protocol however poor adherence to protocol.

**Data analysis**
4. On what parameters you choose different immunotherapy molecules? | 80 | 1 | 6 | 4.15 | 1.584
5. What are your goals for immunotherapy when you prescribe for a patient? | 80 | 1 | 4 | 2.31 | 1.132
6. How long does it take immunotherapy to start? | 80 | 1 | 4 | 2.36 | 1.139
7. Start and what is the duration of therapy? | 80 | 1 | 3 | 2.16 | .818
8. Which medicine has a good activity of immune checkpoint? | 80 | 1 | 4 | 2.41 | 1.052
9. Generally, prescribe PDL inhibitors | 80 | 1 | 4 | 2.31 | 1.132
10. Generally, prescribe PDL-1 inhibitors | 80 | 1 | 4 | 2.53 | 1.136
11. What is the success rate of (%) immunotherapy and how effective you feel? | 80 | 1 | 5 | 2.56 | 1.483
12. Would you like to suggest? | 80 | 1 | 3 | 1.94 | .785
Valid N (listwise) | 80

Hypothesis

Ho = There is no significant association between Choosing therapy and Hospitals

H1 = There is a significant association between Choosing therapy and Hospitals.

Chi-Square Tests

|                | Value | df   | Asymp. Sig (2-sided) |
|----------------|-------|------|-----------------------|
| Pearson Chi-Square | 2.202 | 6    | .900                  |
| N of Valid Cases   | 80    |      |                       |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that $\chi^2 = 2.202, p = 0.90$. This tells us that there is no statistically significant association between Choosing therapy and Hospitals.

2. Why do you choose immunotherapy?

This table allows us to understand that Hospitals VS why do you Choose immunotherapy to 1 and 2.

Hypothesis

H02 = There is no significant association between Choosing immunotherapy and Hospitals

H12 = There is a significant association between Choosing immunotherapy and Hospitals.

Chi-Square Tests

|                | Value | df   | Asymp. Sig (2-sided) |
|----------------|-------|------|-----------------------|
| Pearson Chi-Square | 1.005 | 3    | .800                  |
| N of Valid Cases   | 80    |      |                       |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that $\chi^2 = 1.005, p = 0.80$. This tells us that there is no statistically significant association between Choosing immunotherapy and Hospitals.

3. What is your way of treatment of immunotherapy?

This table allows us to understand that Hospitals VS treatment of immunotherapy to 1 and 2.

Citation: Kumar NR, Alvi S (2021) Understanding immunotherapy and its management. Int J Immunother Cancer Res 7(1): 001-007.
DOI: https://dx.doi.org/10.17352/2455-8591.000030
Hypothesis

H₀₃ = There is no significant association between treatment of immunotherapy and Hospitals

H₁₃ = There is a significant association between treatment of immunotherapy and Hospitals.

Chi-Square Tests

|                | Value  | df | Asymp. Sign (2-sided) |
|----------------|--------|----|----------------------|
| Pearson Chi-Square | 10.498 | 3  | .015                 |
| N of Valid Cases     | 80     |    |                      |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 10.498, p = 0.15 \). This tells us that there is a statistically significant association between treatment of immunotherapy and Hospitals.

4. On what parameters you choose different immunotherapy molecules?

Hypothesis

H₀₄ = There is no significant association between immunotherapy molecules and Hospitals

H₁₄ = There is a significant association between immunotherapy molecules and Hospitals.

Chi-Square Tests

|                | Value  | df | Asymp. Sign (2-sided) |
|----------------|--------|----|----------------------|
| Pearson Chi-Square | 14.882 | 15 | .460                 |
| N of Valid Cases     | 80     |    |                      |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 14.882, p = 0.46 \). This tells us that there is no statistically significant association between immunotherapy molecules and Hospitals.

5. What are your goals for immunotherapy when you prescribe for a patient?

Hypothesis

H₀₅ = There is no significant association between when you prescribe for a patient and Hospitals

H₁₅ = There is a significant association between when you prescribe for a patient and Hospitals.

Chi-Square Tests

|                | Value  | df | Asymp. Sign (2-sided) |
|----------------|--------|----|----------------------|
| Pearson Chi-Square | 6.791  | 9  | .659                 |
| N of Valid Cases     | 80     |    |                      |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 6.791, p = 0.65 \). This tells us that there is no statistically significant association between when you prescribe for a patient and Hospitals.

6. How long does it take immunotherapy to start?

Hypothesis

H₀₆ = There is no significant association between How long does it take immunotherapy to start and Hospitals

H₁₆ = There is a significant association between How long does it take immunotherapy to start and Hospitals.

Chi-Square Tests

|                | Value  | df | Asymp. Sign (2-sided) |
|----------------|--------|----|----------------------|
| Pearson Chi-Square | 10.717 | 9  | .296                 |
| N of Valid Cases     | 80     |    |                      |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 10.717, p = 0.29 \). This tells us that there is no statistically significant association between How long does it take immunotherapy to start and Hospitals.

7. What is the duration of therapy?

Hypothesis

H₀₇ = There is no significant association between the duration of therapy and Hospitals

H₁₇ = There is a significant association between the duration of therapy and Hospitals.

Chi-Square Tests

|                | Value  | df | Asymp. Sign (2-sided) |
|----------------|--------|----|----------------------|
| Pearson Chi-Square | 10.498 | 3  | .015                 |
| N of Valid Cases     | 80     |    |                      |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 10.498, p = 0.15 \). This tells us that there is a statistically significant association between the duration of therapy and Hospitals.

This table allows us to understand that Hospitals VS the duration of therapy to 1, 2, 3 and 4.
Hypothesis

H₀₈ = There is no significant association between duration of therapy and Hospitals

H₁₈ = There is a significant association between duration of therapy and Hospitals

| Chi-Square Tests | Value | df | Asymp. Sign (2-sided) |
|------------------|-------|----|-----------------------|
| Pearson Chi-Square | 6.755* | 6 | .344 |
| N of Valid Cases | 80 | |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 6.755, p = 0.34 \). This tells us that there is no statistically significant association between the duration of therapy and Hospitals.

8. Which medicine has a good activity of immune checkpoint?

| Hospital Name               | 1 | 2 | 3 | 4 | Total |
|-----------------------------|---|---|---|---|-------|
| Apollo                      | 5 | 4 | 5 | 4 | 18    |
| Basavaturakam Indo american | 9 | 2 | 6 | 4 | 21    |
| Omega                       | 3 | 8 | 9 | 3 | 23    |
| Yashodha                    | 4 | 4 | 8 | 2 | 18    |
| Total                       | 21| 18| 28| 13| 80    |

This table allows us to understand that Hospitals VS good activity of immune checkpoint to 1, 2, 3 and 4.

Hypothesis

H₀₉ = There is no significant association between the good activity of immune checkpoint and Hospitals

H₁₉ = There is a significant association between the good activity of immune checkpoint and Hospitals

| Chi-Square Tests | Value | df | Asymp. Sign (2-sided) |
|------------------|-------|----|-----------------------|
| Pearson Chi-Square | 8.998* | 9 | .437 |
| N of Valid Cases | 80 | |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 8.998, p = 0.43 \). This tells us that there is no statistically significant association between medicines has a good activity of immune checkpoint and Hospitals.

8.1 Generally, prescribe PDL inhibitors.

| Hospital Name               | 1 | 2 | 3 | 4 | Total |
|-----------------------------|---|---|---|---|-------|
| Apollo                      | 4 | 6 | 2 | 6 | 18    |
| Basavaturakam Indo american | 9 | 2 | 6 | 4 | 21    |
| Omega                       | 6 | 6 | 5 | 6 | 23    |
| Yashodha                    | 6 | 8 | 3 | 1 | 18    |
| Total                       | 25| 22| 16| 17| 80    |

This table allows us to understand that Hospitals VS Generally, prescribe PDL inhibitors to 1, 2, 3 and 4.

Hypothesis

H₀₁₀ = There is no significant association between Generally, prescribe PDL inhibitors and Hospitals

H₁₁₀ = There is a significant association between Generally, prescribe PDL inhibitors and Hospitals

| Chi-Square Tests | Value | df | Asymp. Sign (2-sided) |
|------------------|-------|----|-----------------------|
| Pearson Chi-Square | 11.424* | 9 | .248 |
| N of Valid Cases | 80 | |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 11.424, p = 0.24 \). This tells us that there is no statistically significant association between Generally, prescribe PDL inhibitors and Hospitals.

8.2 Generally, prescribe PDL-1 inhibitors.

| Hospital Name               | 1 | 2 | 3 | 4 | Total |
|-----------------------------|---|---|---|---|-------|
| Apollo                      | 6 | 4 | 2 | 6 | 18    |
| Basavaturakam Indo american | 9 | 6 | 4 | 5 | 21    |
| Omega                       | 4 | 5 | 7 | 7 | 23    |
| Yashodha                    | 4 | 4 | 7 | 3 | 18    |
| Total                       | 20| 19| 20| 21| 80    |

This table allows us to understand that Hospitals VS Generally, prescribe PDL-1 inhibitors to 1, 2, 3 and 4.

Hypothesis

H₀₁₁ = There is no significant association between generally, prescribe PDL-1 inhibitors and Hospitals

H₁₁₁ = There is a significant association between generally, prescribe PDL-1 inhibitors and Hospitals

| Chi-Square Tests | Value | df | Asymp. Sign (2-sided) |
|------------------|-------|----|-----------------------|
| Pearson Chi-Square | 5.997* | 9 | .740 |
| N of Valid Cases | 80 | |

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 5.997, p = 0.74 \). This tells us that there is no statistically significant association between generally, prescribe PDL-1 inhibitors and Hospitals.

9. What are the side effects of immunotherapy and how do you control them?

| Hospital Name               | 1 | 2 | 3 | 4 | Total |
|-----------------------------|---|---|---|---|-------|
| Apollo                      | 4 | 7 | 5 | 2 | 18    |
| Basavaturakam Indo American | 4 | 9 | 5 | 3 | 21    |
| Omega                       | 7 | 5 | 10| 1 | 23    |
| Yashodha                    | 5 | 2 | 6 | 5 | 18    |
| Total                       | 20| 23| 26| 11| 80    |

This table allows us to understand that Hospitals VS side effects of immunotherapy and control to 1, 2, 3 and 4.
Hypothesis

\( H_{03} = \) There is no significant association between side effects of immunotherapy and control and Hospitals

\( H_{13} = \) There is a significant association between side effects of immunotherapy and control and Hospitals

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 10.737, p = 0.29 \). This tells us that there is no statistically significant association between side effects of immunotherapy and control and Hospitals;

### Chi-Square Tests

| Hospital Name          | Value | df | Asymp. Sign (2-sided) |
|-----------------------|-------|----|-----------------------|
| Apollo                | 5     | 4  | 0.159                 |
| Basavaturakam Indo American | 11   | 2  | 0.212                 |
| Omega                 | 7     | 4  | 0.132                 |
| Yashodha              | 2     | 4  | 0.547                 |
| Total                 | 25    | 11 | 0.159                 |

This table allows us to understand that Hospitals VS success rate of (%) immunotherapy and effective to 1, 2, 3, 4 and 5.

Hypothesis

\( H_{03} = \) There is no significant association between the success rate of (%) immunotherapy and effective and Hospitals

\( H_{13} = \) There is a significant association between the success rate of (%) immunotherapy and effective and Hospitals

When reading this table we are interested in the results of the “Pearson Chi-Square” row.

We can see here that \( \chi^2 = 17.186, p = 0.14 \). This tells us that there is no statistically significant association between the success rate of (%) immunotherapy and effective and Hospitals.

### Chi-Square Tests

| Hospital Name          | Value | df | Asymp. Sign (2-sided) |
|-----------------------|-------|----|-----------------------|
| Apollo                | 12    |    | 0.143                 |
| Basavaturakam Indo American | 16   |    | 0.159                 |
| Omega                 | 23    |    | 0.132                 |
| Yashodha              | 15    |    | 0.547                 |
| Total                 | 80    |    | 0.159                 |

This table allows us to understand that Hospitals VS you like to suggest on existing immunotherapy to 1, 2 and 3.

### Chi-Square Tests

| Hospital Name          | Value | df | Asymp. Sign (2-sided) |
|-----------------------|-------|----|-----------------------|
| Apollo                | 12    |    | 0.143                 |
| Basavaturakam Indo American | 16   |    | 0.159                 |
| Omega                 | 23    |    | 0.132                 |
| Yashodha              | 15    |    | 0.547                 |
| Total                 | 80    |    | 0.159                 |

Conclusion

Based on primary and secondary research the researcher can conclude that a few null hypotheses were estimated previously, their results after the data analysis were estimated. Doctors still need long term studies and observations on immunotherapy to have a specific protocol instead of a global protocol because the immunotherapy came into India in the year between 2013 to 2014. The percentage of people willing to undergo immunotherapy treatment is less. The doctors may choose immunotherapy molecules based on the economic factors and its cost involved in the therapy. They mainly choose immunotherapy because it can be given with any other therapy and has good potential action. In the future, the success rate of immunotherapy will be increasing if it can be used along with any other therapy i.e combination therapy. This would be the upcoming future in immunotherapy. The achievement saw with disease immunotherapy medicines stresses the significance of understanding tumor immunology—especially the parts of tumor antigens and the immunosuppressive tumor microenvironment. Fortunately, numerous new immunotherapy techniques and specialists are being explored and tried in clinical preliminaries, which will ideally give new compelling medicines to patients living with backslid or obstinate malignancies.

References

1. Raval RR, Sharabi AB, Walker AJ, Drake CG, Sharma P (2014) Tumor immunology and cancer immunotherapy: Summary of the 2013 SITC primer. J Immunother Cancer 2: 14. Link: http://bit.ly/3nCcqgr
2. Thappa D, Chiramel M (2016) Evolving role of immunotherapy in the treatment of refractory warts. Indian Dermatology Online Journal 7: 364. Link: http://bit.ly/39mrycK
3. Oiseth SJ, Aziz MS (2017) Cancer immunotherapy: a brief review of the history, possibilities, and challenges ahead. Journal of Cancer Metastasis and Treatment 3: 250. Link: http://bit.ly/3oFxXWl
4. Yu Y, Cui J (2018) Present and future of cancer immunotherapy: A tumour microenvironmental perspective. Oncology Letters Spandidos 16: 4105-4113. Link: http://bit.ly/3owl8Ot
1. Davis AA, Patel VG (2019) The role of PD-L1 expression as a predictive biomarker: An analysis of all US food and drug administration (FDA) approvals of immune checkpoint inhibitors. Journal for Immunotherapy and Cancer Research 7: 278. Link: http://bit.ly/3oCUle3

2. Quintana E, Shackleton M, Sabel MS, Fullen DR, Johnson TM, et al. (2008) Efficient tumour formation by single human melanoma cells. Nature 456: 593-598. Link: http://bit.ly/3oCpJld

3. Yang X, Zeng Q, Barlş M, Tezel G (2020) Transgenic inhibition of astroglial NF-κB restrains the neuroinflammatory and neurodegenerative outcomes of experimental mouse glaucoma. J Neuroinflammation 17: 252. Link: http://bit.ly/38Cp8Ym

4. Thappa DM, Chiramel MJ (2016) The evolving role of immunotherapy in the treatment of refractory warts. Indian Dermatol Online J 7: 364-370. Link: http://bit.ly/3i2t5sp

5. Jackson HA, Jackson MW, Coblentz L, Hammerberg B (2003) Evaluation of the clinical and allergen-specific serum immunoglobulin E responses to oral challenge with cornstarch, corn, soy and a soy hydrolysate diet in dogs with a spontaneous food allergy. Vet Dermatol 4: 181-187. Link: http://bit.ly/3q3ZTUC

6. Vinuya RZ (2000) Specific Allergen Immunotherapy for Allergic Rhinitis and Asthma. Pediatric Annals 29: 425-432. Link: http://bit.ly/38zPQR4

7. Alsaab HO, Sau S, Alzhrani R, Tatiparti K, Bhise K, et al. (2017) PD-1 and PD-L1 checkpoint signalling inhibition for cancer immunotherapy: mechanism, combinations, and clinical outcome. Front Pharmacol 8: 561. Link: http://bit.ly/39uct98

8. Narváez J, Juarez-López P, LLuch J, Narváez JA, Palmero R, et al. (2018) Rheumatic immune-related adverse events in patients on anti-PD-1 inhibitors: fasciitis with myositis syndrome as a new complication of immunotherapy. Autoimmun Rev 17: 1040-1045. Link: http://bit.ly/38yCHYA

9. Andrews LP, Yano H, Vignali DA (2019) Inhibitory receptors and ligands beyond PD-1, PD-L1 and CTLA-4: breakthroughs or backups. Nature immunology 20:1425-1434. Link: https://go.nature.com/2XwGKyh.