

Estimating U.S. Government Cost Savings Associated with Rescuing Transplanted Kidneys Before Chronic Rejection by Employing ImmunoFree Treatments

Executive Summary:

Approximately 5,000 kidney grafts fail (death censored) each year in the United States causing the transplant patient to go back on dialysis or get another transplant. About 3,000 or 63% of these graft failures are due to chronic rejection. ImmunoFree provides a treatment that can cure approximately 80% of patients (2,400) facing chronic rejection and allow those patients to permanently discontinue Immunosuppressant medication. As a results, if the ImmunoFree treatment were given to 2,400 patients per year, this paper shows that the U.S. Government could save approximately \$1.5 billion annually or about \$608,000 per patient treated.

Introduction and Statement of Purpose:

Some transplanted kidneys fail resulting in the need for the patient to go on dialysis, receive another transplant or die due to complications of graft failure. Between 15 and 28 percent of kidney transplants result in some form of graft rejection within five years after transplant and 63% of graft failures after the first year are due to chronic rejection.¹ The purpose of this paper is to report estimated cost savings to the U. S. Government if ImmunoFree treatments can be used to prevent chronic kidney rejection.

Success of the ImmunoFree tolerance induction protocol is defined as being alive at one year after infusion of IF001, being off all immunosuppressive agents with a normal functioning kidney and with no evidence of either kidney graft rejection or graft-versus-host disease (GVHD). The success rate of the tolerance induction protocol is estimated from the results of similar protocols of partially HLA-mismatched hematopoietic cell transplantation for non-malignant hematologic disorders such as aplastic anemia or sickle cell disease. While there are substantially more data on outcomes of transplantation for hematologic malignancies, transplants for these patients are different because they do not seek to minimize GVHD and post-transplant relapses of the blood cancer confounds interpretation of outcomes.

The ImmunoFree tolerance induction protocol was modeled after a study by DeZern et al in which 20 treatment-naïve patients with aplastic anemia received bone marrow transplants

¹ Hariharan, Sundaram, Ajay Israni, and Garbriel Danovitch, "Long-Term Survival after Kidney Transplant", The New England Journal of Medicine, 2021;385:729-43

from half-matched family donors.² All 20 patients experienced sustained donor engraftment, were cured of their aplastic anemia and were completely off immunosuppression without evidence of GVHD at one year after transplantation. In a more recent report by Kassim et al, 38 adult patients with sickle cell disease received half-matched bone marrow transplants from a family donor. Thirty-six of 38 patients were alive, cured of sickle cell disease, and off all immunosuppression one year after transplantation. There were no subsequent treatment failures after one year in either study.³ Pooling the two studies, the success rate of the ImmunoFree procedure for tolerance induction is estimated at 96.6% (56/58) with a 95% confidence interval of 91.9% - 100% by Clopper-Pearson interval method.

Table 1 summarizes the present value cost savings estimates for three levels of treatment success (90%, 95%, and 98%) and three different numbers of patients treated each year (2,000, 2,400, and 3,000).

Table 1
Cost Savings for ImmunoFree Treatments

		PV Total Cost Savings - Per Year		
		Number of ImmunoFree Treatments Per Year		
ImmunoFree Success Rate	Savings Per Treatment - PV	2,000	2,400	3,000
98%	\$628,000	\$1.26 billion	\$1.51 billion	\$1.88 billion
95%	\$608,000	\$1.22 billion	\$1.46 billion	\$1.83 billion
90%	\$575,000	\$1.15 billion	\$1.38 billion	\$1.73 billion

Based upon the success rate, the number of annual treatments and a series of parameter inputs⁴, the present value total cost savings in Year 1 is projected to be between approximately \$1.15 billion and \$1.88 billion. The present value cost savings per treatment is estimated to be between \$575,000 and \$628,000. Based on a 95% ImmunoFree success rate, the best estimate for the per treatment costs savings is \$608,000.

In addition to the projected quantifiable cost savings resulting from ImmunoFree treatments, there are also significant quality of life benefits to transplant recipients if graft failure can be prevented. This paper addresses only the dollar cost savings.⁵

² DeZern AE, Zahurak M, Symons HJ, et al. Alternative donor BMT with post-transplant cyclophosphamide as initial therapy for acquired severe aplastic anemia. *Blood*. 2023; 141(25):3031-3038

³ Kassim AA, de la Fuente J, Nur E, et al. An international learning collaborative phase 2 trial for haploidentical bone marrow transplant in sickle cell disease. *Blood*. 2024;143(25):2654-2665

⁴ The parameter inputs are summarized in Appendix 1.

⁵ Additional savings to the U.S. Government could accrue from increases in income tax collections from ImmunoFree treated patients who avoid graft failure and are able to continue working.

Graft Failure and the Role of ImmunoFree Treatment:

In 2024 nearly 28,000 kidney transplants were performed in the United States.⁶ A kidney transplant offers the recipient the chance for a longer healthier life. The average number of graft failures annually since 2010 has been nearly 5,000.⁷ Based on the previously referenced paper by Hariharan, Israni, and Danovitch, approximately 63 percent could be attributed to chronic graft rejection symptoms. Of these, it is estimated that 80% will result in graft failure. Thus, on an annual basis, the demand for ImmunoFree treatments to prevent kidney graft rejection from occurring is approximately 2,400.

Chronic rejection can be anticipated by monitoring the strength of the transplant recipient's Donor Specific Antibodies (DSAs).⁸ The measurement of DSAs can be accomplished by completing annual antibody screenings like the method the National Kidney Registry uses for all Kidney for Life transplant recipients. The strength of the DSA is measured in Mean Fluorescence Intensity (MFI). DSAs above 1,000 MFI can be flagged, and if the MFI values trend up, these patients are considered at risk of chronic rejection. In addition to getting a transplant recipient off immunosuppressant medications, successful ImmunoFree treatment has the potential to eliminate the DSAs and halt the chronic graft rejection.

Assumptions and Methodology:

This paper reports on the results of a cost savings analysis associated with ImmunoFree treatments to rescue transplanted kidneys from chronic rejection. This study estimates the cost savings for three levels for patient treatments (2,000, 2,400, and 3,000). A flexible computer model has been developed that provides cost savings calculations for a variety of scenarios. The model calculates two sets of costs: (1) the costs associated with graft failures if ImmunoFree treatments were not administered and (2) the costs associated with providing ImmunoFree treatments.

These cost calculations depend on the assumed number of ImmunoFree treatments administered in year 1 to patients who are predicted to experience graft failure. The main body of this paper assumes 2,400 treatments. The cost savings results also depend on the projected success rate of the ImmunoFree treatment in preventing the graft failure. Three success rates

⁶ <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#>

⁷ August 2024 SRTR standard analysis file.

⁸ Diebold, Matthias MD^{1,2}; Mayer, Katharina A. MD¹; Hidalgo, Luis PhD³; Kozakowski, Nicolas MD⁴; Budde, Klemens MD⁵; Böhmig, Georg A. MD¹. Chronic Rejection After Kidney Transplantation. Transplantation ():10.1097/TP.0000000000005187, August 28, 2024. | DOI: 10.1097/TP.0000000000005187

are examined: 90%, 95%, and 98%. In addition the costs also depend on several key input parameters (Appendix 1) discussed in the following sections of this paper.

Costs When ImmunoFree Treatments Are Not Provided

Without the ImmunoFree treatment, a patient with graft failure will either return to dialysis treatment or die because of the graft failure. This study assumes that 80% (1,920) of the 2,400 patients will return to dialysis.

Post Graft Dialysis Costs: The cost of dialysis treatments is reimbursed by Medicare. Based upon data obtained through the United States Renal Data System (USRDS), in 2021 the average annual per patient Medicare payment for dialysis treatment was between \$87,000 and \$99,000 depending on the type of dialysis.⁹ This paper assumes a Year 1 annual dialysis cost of \$100,000 per year. Further, it is assumed that these patients will stay on dialysis for an average of three years before receiving a second transplant. Appendix 2 shows the methodology used to calculate \$593 million dialysis costs for 1,920 dialysis patients following graft failure.

Post-Graft Death Costs: While 80% of graft patients who experience graft failure return to dialysis, 20% are assumed to die. Appendix 3 shows the death cost calculations assuming an average death cost of \$150,000. The total death cost in the current year for 480 deceased patients is projected to be \$72 million.

Post- Graft Failure Disability Costs: In addition to incurring dialysis treatment costs, many dialysis patients are unable to work and are eligible for federal disability payments. Based on a National Institute of Health study, the percentage of ESRD patients receiving disability benefits in 2022 was 67%.¹⁰ The Social Security Administration estimates that the average disability benefit is \$18,000 annually.¹¹ Appendix 4 provides the calculation methods for the \$71.6 million total disability calculation.

Graft Failure Medical Costs: Transplant patients who experience chronic graft rejection begin to incur graft failure costs about three months prior and for at least one month following graft failure. Based on USRDS data, Cooper et al reported that these costs average about \$150,000 per patient.¹² Based on a 2,400-graft failure scenario, the total cost for the medical costs directly related to graft failure is \$360 million.

⁹ https://journals.lww.com/kidney360/fulltext/2021/11000/global_perspective_on_kidney_transplantation_.20.aspx

¹⁰ www.google.com/search?client=firefox-b-1-d&q=percentage+of+dialysis+patients+on+disability+benefits#vhid=zephyr:0&vssid=atritem-https://pmc.ncbi.nlm.nih.gov/articles/PMC10090013/, Sustained employment, work disability and work functioning in CKR patients: a cross-sectional survey study

¹¹ <https://www.ssa.gov/oact/STATS/dib-g3.html>

¹² Cooper M, Schnitzler M, Nilubol C, Wang W, Wu Z, Nordyke RJ. Costs in the Year Following Deceased Donor Kidney Transplantation: Relationships With Renal Function and Graft Failure. *Transpl Int.* 2022 May 27;35:10422. doi: 10.3389/ti.2022.10422. PMID: 35692736; PMCID: PMC9184448.

Graft Failure Re-Transplant Costs: This paper assumes that all patients who experience graft failure and who go on dialysis will receive a second transplant in an average of 3 years following graft failure. There is considerable variability in reported costs associated with the medical services required for a kidney transplant. For instance, a 2018 article authored by Axelrod et al in the *American Journal of Transplantation* stated that the average cost of a live donor kidney transplant (LDKT) was \$94,000.¹³ A 2015 study authored by Held, et al published in the same journal pegged the average kidney transplant cost at \$145,000.¹⁴ A 2022 article by McCormick et al reported an average transplant cost of \$114,000.¹⁵ For the purposes of this study, a total cost associated with a second transplant is \$135,000. Appendix 5 shows the calculation methods required to provide a total second transplant cost of \$275 million.

OACC Pre-Transplant Costs: Costs that are incurred pre-transplant and directly related to the transplant are reported to the Organ Acquisition Cost Center (OACC). Included in the total pre-transplant cost report are such services as nurse coordination and social worker visits, diagnostic testing including histocompatibility testing, behind-the-scenes operations including up-dating the patient's health status, processing deceased organ offers, and post-donation care of living donors.¹⁶ A 2019 paper by Schold, Arrigain, and Fletcher reports that the median annual OACC cost in 2017 was \$100,000.¹⁷ Using a 3 percent medical inflation rate, the 2025 OACC cost is estimated to be \$125,000. Appendix 6 shows the calculation steps to arrive at a total OACC pre-transplant cost of \$255 million.

Post-Second Transplant Immunosuppressant Therapy Costs: Following the second transplant, patients go on immunosuppressant therapy. This paper assumes that these patients will continue these treatments for 20 years post-transplant. Most sources including the USRDS show that the average per patient Medicare payment for post-transplant immunosuppression treatment is between \$25,000 and \$30,000 per year. For the purposes of this study this cost is set at \$25,000. Appendix 7 shows the methodology for calculating the \$1.4 billion immunotherapy cost over 20 years following the second transplant.

Medical Complication Costs While on Immunotherapy: Many patients who have received a kidney transplant and are on immunosuppressant therapy can be expected to incur health related costs that are covered by Medicare. This paper assumes that 90% of patients on immunotherapy incur these costs and the annual cost per patient is \$10,000. Appendix 8

¹³ Axelrod DA, Schnitzler MA, Xiao H, Irish W, Tuttle-Newhall E, Chang SH, Kasiske BL, Alhamad T, Lentine KL. An economic assessment of contemporary kidney transplant practice. *Am J Transplant*. 2018 May;18(5):1168-1176. doi: 10.1111/ajt.14702. Epub 2018 Mar 31. PMID: 29451350..

¹⁴ Held, P.J., F. McCormick, A. Ajo, and J.P. Roberts, A Cost-Benefit Analysis of Government Compensation of Kidney Donors, *American Journal of Transplantation*, 2015.

¹⁵ McCormick, et. al, Projecting the Economic Impact of Compensating Living Kidney in the United States: Cost-Benefit Analysis Demonstrates Substantial Patient and Societal Gains, *ScienceDirect*, Volume 25, Issue 12, 2022.

¹⁶ Xu, Kunyao, et. al., The Medical Costs of Determining Eligibility and Waiting for a Kidney Transplantation, *Med Care* Volume 62, Number 8, 2024 (Wolters Kluwer Health, Inc.)

¹⁷ Schold JD, Arrigain S, Flechner SM, et al. Dramatic secular changes in prognosis for kidney transplant candidates in the United States. *Am J Transplant*. 2019;19:414–424.

displays the calculation methods for determining the 20-year total immunotherapy complications cost. The total cost is \$507 million.

Total Costs - Not Using ImmunoFree Treatments to Prevent Graft Rejection:

Based on the scenario assumptions introduced in this paper, the previous sections showed the costs for 2,400 patients who experienced graft rejection but did not receive ImmunoFree treatments. Table 2 summarizes these cost calculations. The total cost for this scenario is shown to be \$3.5 billion. A typical person who survives graft failure would be expected to incur the following costs:

Graft Failure Medical Cost =	\$150,000
Dialysis Cost (3 years) =	\$300,000
Disability Cost (3 years) =	\$ 36,000
Re-Transplant (3 rd Year) Cost =	\$140,000
OACC Pre-transplant (3 rd Year) Cost =	\$125,000
Immuno Therapy Cost (20 Years) =	\$730,000
Medical Complications (20 Years) =	<u>\$260,000</u>
Total Cost ¹⁸ =	\$1,741,000

Table 2
Total Costs for 2,400 Patients with Rejected Grafts

Costs Associated With Chronic Kidney Failure		
No ImmunoFree Treatment		
Patients With Chronic Post Transplant Kidney Failure	2400	
Number of Patients Returning to Dialysis	1920	
Number of Patient Deaths Following Graft Failure	480	
Post Graft Failure Dialysis Cost		\$593,452,800
Post Graft Failure Death Cost		\$72,000,000
Post Graft Failure Disability Cost		\$71,570,408
Graft Failure Medical Costs (3 months prior through Year 1 following)		\$360,000,000
Graft Failure Re-Transplant Cost		\$274,985,280
OACC Costs - Pre-Transplant		\$254,616,000
Immuno Therapy Costs Post 2nd Transplant - Next 20 years		\$1,409,375,218
Medical Complication Cost While on Immuno Therapy - Next 20 Years		<u>\$507,375,078</u>
Total Costs - No ImmunoFree Treatment		\$3,543,374,784

¹⁸ Values rounded to nearest thousands.

Costs When ImmunoFree Treatments Are Provided

Given the scenario of specific inputs and assumptions to the cost model (See Appendix 1), the previous section projected a \$3.5 billion total costs to the U.S. Government assuming no ImmunoFree treatments were made available to protect grafts from being rejected. However, the proposal is to administer ImmunoFree treatments to patients at risk of chronic graft rejection when Donor Specific Antibodies (DSAs) edge above 1,000 and with Mean Fluorescence Intensity (MFI) readings trending upwards. Furthermore, the proposal is for Medicare to pay for the direct ImmunoFree treatment costs plus all other kidney transplant related costs currently paid by Medicare or other U.S. Government departments. Consequently, it is important to estimate the cost savings the U.S. Government would accrue under this proposal. This requires that the costs associated with providing 2,400 ImmunoFree treatments be estimated and compared to the \$3.5 billion cost if no treatments are provided.¹⁹

An important element in calculating the costs associated with the ImmunoFree treatments is the treatment success rate. The justification behind the success rates was introduced earlier. This paper considers three different levels of success: 90%, 95%, and 98% with the most likely rate being 95%. The cost calculations also assume that 2,400 treatments will be administered, 80% of patients experiencing unsuccessful treatments will go on dialysis for 3 years until receiving a second transplant, and 95% of successful treatments will result in transplant patients going off Immunosuppressant medications as a result from having been administered the ImmunoFree treatment.

For a 95% success rate of the 2,400 patients receiving ImmunoFree treatments, 2,280 patients will have their grafts saved. Of the 120 unsuccessful treatments, 96 patients are assumed to go back on dialysis for three years at which point they will receive a second transplant. The other 24 patients are assumed to have died because of graft failure. Finally, of the 2,280 successful ImmunoFree treatments 2,166 patients are assumed to no longer need immunotherapy treatments. Table 3 shows the patient breakdown for each of the three success rates being considered in this paper.

Table 3
ImmunoFree Treatment Patient Breakdown

	90% Success	95% Success	98% Success
Transplant Patients Receiving Immuno Free Treatments	2400	2400	2400
Successful Graft Rescues From Treatments	2160	2280	2352
Number of Unsuccessful Graft Rescues Going Back on Dialysis	192	96	38
Number of Unsuccessful Graft Rescues Going on Disability	129	64	25
Number of Unsuccessful Graft Rescues Who Die	48	24	10
Number of Patients Freed from Immunosuppressant Treatments	2052	2166	2234

¹⁹ Cost savings results for 1,000, 2,000, 3,000, 4,000 and 5,000 ImmunoFree treatments are shown later in this paper.

ImmunoFree Treatment Costs: There are three specific assumed costs directly associated with each ImmunoFree Treatment; (1) \$150,000 cost for Apheresis & Stem Cell Processing, (2) \$150,000 Hospital & Follow-up cost, and (3) \$50,000 desensitization cost. These costs are all incurred in Year 1 regardless of whether the treatment is a success. For 2,400 ImmunoFree treatments, the total Apheresis & Stem Cell Processing Cost is \$360 million ($2,400 \times \$150,000 = \$360,000,000$). The total Hospital & Follow-up cost is \$360 million ($2,400 \times \$150,000 = \$360,000,000$) and the total Desensitization cost is \$120 million ($2,400 \times \$50,000 = \$120,000,000$). The total cost for these ImmunoFree treatment components is \$840 million.

Dialysis Cost for Failed ImmunoFree Treatments: A patient who survives graft failure following unsuccessful ImmunoFree treatments will go on dialysis for an average of 3 years before receiving a second transplant. Appendix 9 shows the dialysis cost calculations. Total dialysis costs for the 90%, 95% and 98% ImmunoFree success rates are \$60 million, \$30 million and \$12 million respectively.

Death Cost for Failed ImmunoFree Treatments: In cases where the ImmunoFree treatment proves unsuccessful in preventing graft failure, the scenario utilized in this paper assumes that 20 percent of those who experience graft failure will die. Table 3 shows that if the ImmunoFree treatment success rate is 90%, the number of deaths is expected to be 48. For a 95% success rate, 24 patients are expected to die and for 98% success, the number of deaths is projected to be 10. The assumed Medicare cost associated with a death is \$150,000. Then, for the 90%, 95% and 98% treatment success rates, the total death costs are projected to be \$7.2 ($48 \times \$150,000$) million, \$3.6 million ($24 \times \$150,000$) and \$1.5 million ($10 \times \$150,000$).

Disability Cost for Dialysis Patients Post-Graft Failure: Previously this paper reported studies showing that 67% of dialysis patients go on disability at an average annual disability cost to the U.S. Government is \$18,000 per person. Appendix 10 shows the calculations for the total disability costs of \$7.2 million, \$3.6 million, and \$1.4 million for ImmunoFree success rates of 90%, 95% and 98% respectively.

Graft Failure Medical Costs: Transplant patients who experience chronic graft rejection begin to incur graft failure costs about three months prior and for at least one month following graft failure. Based on USRDS data, Cooper et al reported that these costs average about \$150,000 per patient.²⁰ Based on 2,400-ImmunoFree treatments, 90% success rate and 240 expected graft failures the total medical cost directly related to graft failure is \$36 million. For a 95% success rate, the total medical cost associated with 120 graft failures is \$18 million and \$7.2 million for a 98% success rate.

²⁰ Cooper M, Schnitzler M, Nilubol C, Wang W, Wu Z, Nurdyke RJ. Costs in the Year Following Deceased Donor Kidney Transplantation: Relationships With Renal Function and Graft Failure. *Transpl Int.* 2022 May 27;35:10422. doi: 10.3389/ti.2022.10422. PMID: 35692736; PMCID: PMC9184448.

Re-Transplant Cost for Graft Rejection Patients: This paper assumes that 80% of patients whose ImmunoFree treatment was unsuccessful and who survived graft failure will receive a second transplant 3 years on average after their graft failed. The cost of a second transplant is assumed to be \$135,000. Appendix 11 shows the calculations showing the total re-transplant costs for each of the potential ImmunoFree treatment success rates as \$27.5 million, \$13.7 million, and \$5.5 million.

OACC Pre-Transplant Cost: The median pre-transplant cost reported to OACC is assumed to be \$125,000. Appendix 12 presents the calculation methods used to arrive at total OACC pre-transplant costs of \$25.5 million, \$12.7 million, and \$5.1 million for the 90%, 95%, and 98% ImmunoFree graft rescue success rates.

Immunosuppressant Therapy Cost – Post second Transplant Over 20 Years: The ImmunoFree treatment has two objectives. One is to prevent graft rejection and the second is to allow transplant patients to discontinue immunosuppressant treatments post-transplant. The scenario utilized in this paper assumes that 95% of transplant patients will be free of immunosuppressant therapy even if the ImmunoFree treatment is not successful in preventing graft rejection. Thus 5% of patients who receive a second transplant will continue to require immunosuppressant therapy at an annual cost of \$25,000 for 20 years. Appendix 13 displays the immunosuppressant cost calculation methodology. The total immunosuppressant costs for the 90%, 95%, and 98% ImmunoFree graft rescue success rates are \$7 million, \$3.5 million, and \$1.4 million.

Medical Complications Cost – Patients on Immunosuppressants: The scenario considered in this paper assumes that 90% of patients who received a second transplant and who are on immunosuppressant medications will experience side effects at an annual cost of \$10,000. Appendix 14 shows the calculation methods to determine the total medical complication cost over 20 years for all patients who remain on Immunosuppressant medications following their second transplant. The total medical complications costs for a 90%, 95%, and 98% ImmunoFree success rate are \$50.7 million, \$25.4 million, and \$10.1 million.

Total Costs - Using ImmunoFree Treatments to Prevent Graft Rejection: The previous sections showed the various costs assuming 2,400 patients received ImmunoFree treatments. Table 4 summarizes these cost calculations for three assumed ImmunoFree success levels (90%, 95%, and 98%). The total cost ranges from \$884 million to \$1.06 billion.

Table 4
Total Costs Associated With 2,400 Patients Treated

	90% Success	95% Success	98% Success
ImmunoFree Costs for Apheresis & Stem Cell Processing	\$360,000,000	\$360,000,000	\$360,000,000
ImmunoFree Center, Hospital and Follow-up Costs	\$360,000,000	\$360,000,000	\$360,000,000
ImmunoFree Desensitization Cost	\$120,000,000	\$120,000,000	\$120,000,000
Post ImmunoFree Graft Failure Dialysis Cost	\$59,345,280	\$29,672,640	\$11,869,056
Post ImmunoFree Graft Failure Death Cost	\$7,200,000	\$3,600,000	\$1,440,000
Post Graft Failure Disability Cost	\$7,157,041	\$3,578,520	\$1,431,408
Graft Failure Medical Costs (3 months prior through Year 1 following)	\$36,000,000	\$18,000,000	\$7,200,000
Post ImmunoFree Graft Failure Re-Transplant Cost	\$27,498,528	\$13,749,264	\$5,499,706
OACC Costs - Pre-Transplant	\$25,461,600	\$12,730,800	\$5,092,320
Immuno Therapy Cost Post 2nd Transplant - Next 20 years	\$7,046,876	\$3,523,438	\$1,409,375
20 Years Medical Complication Cost While on Immuno Therapy	\$50,737,508	\$25,368,754	\$10,147,502
Total ImmunoFree Treatment Related Costs	\$1,060,446,833	\$950,223,416	\$884,089,367

A typical individual who experienced chronic graft rejection symptoms but had a successful ImmunoFree treatment before graft failure would expect to incur the following costs:

ImmunoFree Costs for Apheresis & Stem Cell Processing =	\$150,000
ImmunoFree Center, Hospital and Follow-up Costs =	\$150,000
ImmunoFree Desensitization Cost =	<u>\$ 50,000</u>
Total Cost =	\$350,000

A successfully treated patient would not experience graft failure. As a result, the patient would not go on dialysis, would not need a second transplant, would not go on disability, would no longer require immunosuppressant medications or incur additional medical costs due to receiving Immunotherapy.

ImmunoFree Cost Savings Summary

The purpose of this paper is to report results of a study to determine projected savings to the U.S. Government by using ImmunoFree treatments to prevent imminent kidney graft failure for patients with severe chronic kidney rejection symptoms. Savings are determined by directly comparing the costs associated with not employing the treatments to the costs if the treatments are applied. Based on a series of defined assumptions, earlier sections of this paper showed that the total cost of not providing ImmunoFree treatments to 2,400 patients is approximately \$3.5 billion. The cost if treatment is provided ranges from \$884 million to \$1.06 billion depending on the treatment's success rate. Table 5 summarizes the cost savings calculations and shows the present value for total savings and individual treatment savings.

As shown in Table 5, when the ImmunoFree treatment for 2,400 patients is 90% successful in preventing graft rejection, using a 4% discount rate the present value for total savings is \$1.7 billion and a per-treatment savings is \$717,000. At a 95% success rate, the present value for total savings is \$1.8 billion and \$753,000 per-treatment. Finally, if the ImmunoFree treatment success rate reaches 98%, the present value total savings is \$1.86 billion with a per-treatment savings of \$774,000.

Table 5
Cost Savings Results – 2,400 ImmunoFree Treatments

	Costs Associated With Chronic Kidney Failure		
	No ImmunoFree Treatment		
	90% Success	95% Success	98% Success
Patients With Chronic Post Transplant Kidney Failure	2400	2400	2400
Number of Patients Returning to Dialysis	1920	1920	1920
Number of Patient Deaths Following Graft Failure	480	480	480
Post Graft Failure Dialysis Cost	\$593,452,800	\$593,452,800	\$593,452,800
Post Graft Failure Death Cost	\$72,000,000	\$72,000,000	\$72,000,000
Post Graft Failure Disability Cost	\$71,570,408	\$71,570,408	\$71,570,408
Graft Failure Medical Costs (3 months prior through Year 1 following)	\$360,000,000	\$360,000,000	\$360,000,000
Graft Failure Re-Transplant Cost	\$274,985,280	\$274,985,280	\$274,985,280
OACC Costs - Pre-Transplant	\$254,616,000	\$254,616,000	\$254,616,000
Immuno Therapy Costs Post 2nd Transplant - Next 20 years	\$1,409,375,218	\$1,409,375,218	\$1,409,375,218
Medical Complication Cost While on Immuno Therapy - Next 20 Years	\$507,375,078	\$507,375,078	\$507,375,078
Total Costs - No ImmunoFree Treatment	\$3,543,374,784	\$3,543,374,784	\$3,543,374,784
	Costs Associated With Chronic Kidney Failure		
	With ImmunoFree Treatment		
	90% Success	95% Success	98% Success
Transplant Patients Receiving Immuno Free Treatments	2400	2400	2400
Successful Graft Rescues From Treatments	2160	2280	2352
Number of Unsuccessful Graft Rescues Going Back on Dialysis	192	96	38
Number of Unsuccessful Graft Rescues Who Die	48	24	10
Number of Patients Freed from Immunosuppressant Treatments	2052	2166	2234
ImmunoFree Costs for Apheresis & Stem Cell Processing	\$360,000,000	\$360,000,000	\$360,000,000
ImmunoFree Center, Hospital and Follow-up Costs	\$360,000,000	\$360,000,000	\$360,000,000
ImmunoFree Desensitization Cost	\$120,000,000	\$120,000,000	\$120,000,000
Post ImmunoFree Graft Failure Dialysis Cost	\$59,345,280	\$29,672,640	\$11,869,056
Post ImmunoFree Graft Failure Death Cost	\$7,200,000	\$3,600,000	\$1,440,000
Post Graft Failure Disability Cost	\$7,157,041	\$3,578,520	\$1,431,408
Graft Failure Medical Costs (3 months prior through Year 1 following)	\$36,000,000	\$18,000,000	\$7,200,000
Post ImmunoFree Graft Failure Re-Transplant Cost	\$27,498,528	\$13,749,264	\$5,499,706
OACC Costs - Pre-Transplant	\$25,461,600	\$12,730,800	\$5,092,320
Immuno Therapy Cost Post 2nd Transplant - Next 20 years	\$7,046,876	\$3,523,438	\$1,409,375
20 Years Medical Complication Cost While on Immuno Therapy	\$50,737,508	\$25,368,754	\$10,147,502
Total ImmunoFree Treatment Related Costs	\$1,060,446,833	\$950,223,416	\$884,089,367
Total Savings From ImmunoFree Treatments	\$2,482,927,951	\$2,593,151,368	\$2,659,285,417
Total Savings Per ImmunoFree Treated Patient	\$1,034,553	\$1,080,480	\$1,108,036
Total Savings From ImmunoFree Treatments - Present Value	\$1,380,664,774	\$1,460,137,016	\$1,507,820,361
Total Savings Per ImmunoFree Treated Patient - Present Value	\$575,277	\$608,390	\$628,258

Although the discussion and cost savings calculations set forth in this paper have assumed 2,400 potential ImmunoFree treatments in Year 1, the cost savings model allows the number of treatments to be adjusted. Table 6 presents a summary of the present value of total cost savings and per-treatment savings for annual treatment levels of 2,000, 2,400, and 3,000. Total present value savings range from a low of \$1.15 billion if only 2,000 ImmunoFree treatments are performed and success rate of only 90% to a high of \$1.88 billion if 3,000 treatments are performed and the treatment success rate reaches 98%. The present value cost savings per treatment range from \$575,000 to \$628,000.

The results presented in this paper demonstrate that the U.S. Government can expect to receive significant savings by funding ImmunoFree treatments to previously transplanted patients who are experiencing chronic graft rejection symptoms. It should be noted that the cost savings reported in this paper are for ImmunoFree treatments administered within one

year only. Similar cost savings to the U.S. Government will occur within all subsequent years in which the treatments are provided to patients with chronic graft rejection symptoms.

Table 6
Cost Savings Summary

ImmunoFree Success Rate	Savings Per Treatment - PV	PV Total Cost Savings - Per Year		
		Number of ImmunoFree Treatments Per Year		
		2,000	2,400	3,000
98%	\$628,000	\$1.26 billion	\$1.51 billion	\$1.88 billion
95%	\$608,000	\$1.22 billion	\$1.46 billion	\$1.83 billion
90%	\$575,000	\$1.15 billion	\$1.38 billion	\$1.73 billion

Appendix – 1

Cost Savings Model - Parameters

Parameter Inputs	
Number of Transplant Patients with Chronic Graft Failure Treated with Immuno Therapy	2400
ImmunoFree Therapy Graft Survival Success Rate	95.0%
Percentage of Graft Failure Patients Who Go Back to Dialysis Versus Death	80.0%
Annual Dialysis Cost	\$100,000
Average Years Until 2nd Transplant (Maximum = 5 Years)	3
Post Graft Failure - 2nd Transplant Costs)	\$135,000
OACC Costs - Pre-Transplant	\$125,000
Graft Failure Medical Costs (3 months prior through Year 1 following)	\$150,000
Medical Complication Cost While on Immuno Therapy	\$10,000
Cost Per Death After Transplant	\$150,000
Immunosuppressant Annual Cost	\$25,000
Immuno Free Costs for Apheresis & Stem Cell Processing	\$150,000
Immuno Free Center, Hospital and Follow-up Costs	\$150,000
Immuno Free Desensitization Cost	\$50,000
Medical Cost Inflation Rate	3.0%
Discount Rate	4.0%
Percentage of LDKT Patients Who Experience Side Effects While on Immuno Therapy	90.00%
ImmunoFree Therapy - Off Immunosuppressants Success Rate	95.00%
Proportion of Dialysis Patients on Disability	67.0%
Annual Disability Cost Per Person	\$18,000

Appendix – 2

Dialysis Cost Calculation Method

Assume that the annual dialysis cost to Medicare for a ESRD patient is \$100,000 and the number of patients that could have been, but were not, provided ImmunoFree treatments is 2,400. The percentage of these patients that return to dialysis is 80%. The medical cost inflation rate is assumed to be 3%

Year 1 Calculation: The Year 1 dialysis costs is computed as follows:

The number of patients returning to dialysis in Year 1 is:

$$2,400 \times .80 = 1,920$$

The Year 1 dialysis cost is

$$1,920 \times \$100,000 = \$192,000,000$$

Because graft fail patients are assumed to be on dialysis for three years until receiving a second transplant, we calculate Year 2 and Year 3 dialysis costs as follows:

Year 2 cost is

$$1,920 \times \$100,000 \times (1.03) = \$197,760,000$$

Year 3 cost is

$$1,920 \times \$100,000 \times (1.03)^2 = \$203,692,800$$

The total three-year dialysis costs is \$593,452,800

Appendix – 3

Death Cost Calculations

Of the 2,400 patients with graft failure, 20% are assumed to die. The cost associated with these deaths is:

$$2,400 \times .20 = 480 \text{ deaths}$$

Using a per person death cost of \$150,000, the total death cost is:

$$480 \times \$150,000 = \$72,000,000$$

Appendix – 4

Disability Cost Calculation Method

Assume that the average annual disability cost to the Federal Government is \$18,000 per person. Appendix 1 showed that the number of graft failure patients is 1,920. The percentage of these patients that will go on disability is 67%. The medical cost inflation rate is assumed to be 3%

Year 1 Calculation: The Year 1 disability costs is computed as follows:

The number of patients on disability in Year 1 is:

$$1,920 \times .67 = 1,286$$

The Year 1 disability cost is

$$1,286 \times \$18,000 = \$23,155,200$$

Because these disability patients are assumed to be on disability for three years until receiving a second transplant, we calculate Year 2 and Year 3 dialysis costs as follows:

Year 2 cost is

$$1,286 \times \$18,000 \times (1.03) = \$23,849,856$$

Year 3 cost is

$$1,286 \times \$18,000 \times (1.03)^2 = \$24,565,352$$

Then total dialysis costs is \$71,570,408

Appendix – 5

Post-Graft Failure Second Transplant Cost Calculations

Appendix 2 showed that the number of patients going on dialysis from the 2,400 graft failure patients is projected to be 1,920. These same patients are projected to get a second transplant on average 3 years following the graft failure. Using a medical inflation rate of 3%, and a Year 1 cost for a transplant of \$135,000, the total second transplant cost is calculated as follows:

The per-transplant cost in year 3 following graft failure is:

$$\$135,000 \times (1.03)^3 = \$143,221$$

Then the total second transplant cost is:

$$1,920 \times \$143,221 = \$274,985,280$$

Appendix – 6

OACC Pre-Second Transplant Cost Calculations

Appendix 2 showed that the number of patients going on dialysis from the 2,400 graft failure patients is projected to be 1,920. These same patients are projected to get a second transplant on average 3 years following the graft failure. Using a medical inflation rate of 3%, and a Year 1 OACC cost of \$125,000, the total second transplant cost is calculated as follows:

The per-transplant cost in year 3 following graft failure is:

$$\$125,000 \times (1.03)^3 = \$132,612$$

Then the total second transplant cost is:

$$1,920 \times \$132,612 = \$254,616,000$$

Appendix – 7

Post-Transplant Immunotherapy Cost Calculations

A patient's annual cost of immunosuppression treatment is set at \$25,000 in Year 1 and the medical inflation rate is assumed to be 3%. All transplants are assumed to have occurred by the end of Year 3. The number of patients requiring Immunotherapy after the second transplant is 1,920.

Year 4 Cost Calculations:

Transplanted patients begin immunotherapy as soon as they receive the transplant, and it continues for as long as the patient lives. For this study, it is assumed that all transplant patients live at least 20 years post-transplant. The immunotherapy treatment costs for the 1,920 patients transplanted in Year 3 are assumed to begin in Year 4

$$1,920 \times \$25,000 \times (1.03)^3 = \$52,450,896$$

Year 5 Cost Calculations:

All transplanted patients except for those whose grafts have failed will continue with immunotherapy medications in Year 5. Year 5 immunosuppressant total cost is:

$$2,400 \times \$25,000 \times (1.03)^4 = \$54,024,423$$

Year 6-23 calculations are done in the same manner. The total cost for years 4-23 is \$1,409,375,218.

Appendix – 8

Medical Costs While on Immunotherapy

Assuming the annual cost of immunotherapy complications is \$10,000 beginning in the year following the second transplant, these costs extend for 20 years, 90% of the patients incur the costs, and the medical inflation rate is 3%, the cost calculations are:

Year 4 cost calculations:

$$1,920 \times .90 \times \$10,000 \times (1.03)^3 = \$18,882,323$$

Year 5 cost calculations:

$$1,920 \times .90 \times \$10,000 \times (1.03)^4 = \$19,448,792$$

Calculations for years 6-23 are performed in the same way giving a 20-year total cost of \$507,375,078.

Appendix – 9

Dialysis Costs for Unsuccessful ImmunoFree Treatments

Assuming 2,400 treatments, a Year 1 (2025) annual dialysis cost of \$100,000, and a 3% inflation rate, the dialysis cost calculations for the 90%, 95%, and 98% success rates are as follows:

90% Success – Table 3 shows that 192 patients are expected to go on dialysis.

$$\text{Year 1 cost: } 192 \times \$100,000 = \$19,200,000$$

$$\text{Year 2 cost: } 192 \times \$100,000 \times (1.03) = \$19,776,000$$

$$\text{Year 3 cost: } 192 \times \$100,000 \times (1.03)^2 = \$20,369,280$$

$$\text{Total Cost} = \$59,345,280$$

95% Success – Table 3 shows that 96 patients are expected to go on dialysis

$$\text{Year 1 cost: } 96 \times \$100,000 = \$9,600,000$$

$$\text{Year 2 cost: } 96 \times \$100,000 \times (1.03) = \$9,888,000$$

$$\text{Year 3 cost: } 120 \times \$100,000 \times (1.03)^2 = \$10,184,640$$

$$\text{Total Cost} = \$29,672,640$$

95% Success – Table 3 shows that 38 patients²¹ are expected to go on dialysis

$$\text{Year 1 cost: } 38 \times \$100,000 = \$3,800,000$$

$$\text{Year 2 cost: } 38 \times \$100,000 \times (1.03) = \$3,914,000$$

$$\text{Year 3 cost: } 38 \times \$100,000 \times (1.03)^2 = \$4,031,420$$

$$\text{Total Cost} = \$11,869,056$$

²¹ Value rounded from 38.4 to 38

Appendix – 10

Disability Costs for Unsuccessful ImmunoFree Treatments

Assuming 2,400 treatments, a Year 1 annual disability cost of \$18,000, and a 3% inflation rate, the disability cost calculations for the 90%, 95%, and 98% success rates are as follows:

90% Success – Table 3 shows that 192 patients are expected to go on dialysis. Of these patients, 129 (67%) are projected to receive disability payments²²

$$\text{Year 1 cost: } 129 \times \$18,000 = \$2,322,000$$

$$\text{Year 2 cost: } 129 \times \$18,000 \times (1.03) = \$2,391,660$$

$$\text{Year 3 cost: } 129 \times \$18,000 \times (1.03)^2 = \$2,463,410$$

$$\text{Total Cost} = \$7,157,041$$

95% Success – Table 3 shows that 96 patients are expected to go on dialysis. Of these patients, 64 are projected to receive disability payments²³

$$\text{Year 1 cost: } 64 \times \$18,000 = \$1,152,000$$

$$\text{Year 2 cost: } 64 \times \$18,000 \times (1.03) = \$1,186,560$$

$$\text{Year 3 cost: } 64 \times \$18,000 \times (1.03)^2 = \$1,222,157$$

$$\text{Total Cost} = \$3,578,520$$

98% Success – Table 3 shows that 38 patients are expected to go on dialysis. Of these patients, 25 are projected to receive disability payments²⁴

$$\text{Year 1 cost: } 25 \times \$18,000 = \$450,000$$

$$\text{Year 2 cost: } 25 \times \$18,000 \times (1.03) = \$463,500$$

$$\text{Year 3 cost: } 25 \times \$18,000 \times (1.03)^2 = \$477,405$$

$$\text{Total Cost} = \$1,431,408$$

²² Value is rounded to next highest whole number.

²³ Value is rounded to next highest whole number.

²⁴ Value is rounded to nearest whole number.

Appendix – 11

Re-Transplant Costs for Unsuccessful ImmunoFree Treatments

Assuming 2,400 treatments, a Year 1 re-transplant cost of \$135,000, and a 3% inflation rate, the re-transplant cost calculations for the 90%, 95%, and 98% success rates are as follows:

90% Success – Table 3 shows that 192 patients are expected to go on dialysis and require a second transplant in year 3.

$$\text{Year 3 cost: } 192 \times \$135,000 \times (1.03)^2 = \$27,498,528$$

95% Success – Table 3 shows that 96 patients are expected to go on dialysis and require a second transplant in year 3.

$$\text{Year 3 cost: } 96 \times \$135,000 \times (1.03)^2 = \$13,749,264$$

98% Success – Table 3 shows that 38 patients are expected to go on dialysis and require a second transplant in year 3.

$$\text{Year 3 cost: } 38 \times \$135,000 \times (1.03)^2 = \$5,442,417$$

Appendix – 12

OACC Pre-Transplant Cost for Unsuccessful ImmunoFree Treatments

Assuming 2,400 treatments, a Year 1 OACC cost of \$125,000, and a 3% inflation rate, the OACC cost calculations for the 90%, 95%, and 98% success rates are as follows:

90% Success – Table 3 shows that 192 patients are expected to go on dialysis and require a second transplant in year 3.

$$\text{Year 3 cost: } 192 \times \$125,000 \times (1.03)^2 = \$25,461,600$$

95% Success – Table 3 shows that 96 patients are expected to go on dialysis and require a second transplant in year 3.

$$\text{Year 3 cost: } 96 \times \$125,000 \times (1.03)^2 = \$12,730,800$$

98% Success – Table 3 shows that 38 patients are expected to go on dialysis and require a second transplant in year 3.

$$\text{Year 3 cost: } 38 \times \$125,000 \times (1.03)^2 = \$5,092,320$$

Appendix – 13

Immunosuppressant Costs After Second Transplant

Assuming 2,400 treatments, a Year 1 annual Immunotherapy cost of \$25,000, 5% of transplant patients will continue to require Immunotherapy, and a 3% inflation rate, the total Immunosuppressant cost calculations for the 90%, 95%, and 98% success rates are as follows:

90% Success – Table 3 shows that $192 \times .05 = 10$ patients²⁵ are expected to go on dialysis, require a second transplant, and need Immunotherapy beginning in year 4 for 20 years.

$$\text{Year 4 cost: } 10 \times \$25,000 \times (1.03)^3 = \$273,182$$

$$\text{Year 5 cost: } 10 \times \$25,000 \times (1.03)^4 = \$281,377$$

Cost calculations continue through Year 23

$$\text{Total Cost} = \$7,046,876$$

95% Success – Table 3 shows that $96 \times .05 = 5$ patients²⁶ are expected to go on dialysis, require a second transplant, and need Immunotherapy beginning in year 4 for 20 years.

$$\text{Year 4 cost: } 5 \times \$25,000 \times (1.03)^3 = \$136,591$$

$$\text{Year 5 cost: } 5 \times \$25,000 \times (1.03)^4 = \$140,689$$

Cost calculations continue through Year 23

$$\text{Total Cost} = \$3,523,438$$

98% Success – Table 3 shows that $38 \times .05 = 2$ patients²⁷ are expected to go on dialysis, require a second transplant, and need Immuno Therapy beginning in year 4 for 20 years.

$$\text{Year 4 cost: } 2 \times \$25,000 \times (1.03)^3 = \$54,636$$

$$\text{Year 5 cost: } 2 \times \$25,000 \times (1.03)^4 = \$56,275$$

Cost calculations continue through Year 23

$$\text{Total Cost} = \$1,409,375$$

²⁵ Number rounded up to nearest integer value. Actual value is 9.6

²⁶ Number rounded up to nearest integer value. Actual value is 4.8

²⁷ Number rounded to next highest integer number. Actual value is 1.9

Appendix – 14

Medical Side-Effect Costs After Second Transplant

Assuming 2,400 treatments, a Year 1 annual side-effect cost of \$10,000, 90% of transplant patients experience side-effects while on immunosuppressant medications, and a 3% inflation rate, the total Immunosuppressant cost calculations for the 90%, 95%, and 98% success rates are as follows:

90% Success – Table 3 shows that $192 \times .90 = 173$ patients are expected to go on dialysis, require a second transplant, and experience medical side-effects beginning in year 4 for 20 years.

$$\text{Year 4 cost: } 173 \times \$10,000 \times (1.03)^3 = \$1,890,418$$

$$\text{Year 5 cost: } 173 \times \$10,000 \times (1.03)^4 = \$1,947,130$$

Cost calculations continue through Year 23

$$\text{Total Cost} = \$50,737,508$$

95% Success – Table 3 shows that $96 \times .90 = 86$ patients are expected to go on dialysis, require a second transplant, and experience medical side-effects beginning in year 4 for 20 years.

$$\text{Year 4 cost: } 86 \times \$10,000 \times (1.03)^3 = \$939,745$$

$$\text{Year 5 cost: } 86 \times \$10,000 \times (1.03)^4 = \$967,938$$

Cost calculations continue through Year 23

$$\text{Total Cost} = \$25,368,754$$

98% Success – Table 3 shows that $38 \times .90 = 34$ patients²⁸ are expected to go on dialysis, require a second transplant, and experience medical side-effects beginning in year 4 for 20 years.

$$\text{Year 4 cost: } 34 \times \$10,000 \times (1.03)^3 = \$371,527$$

$$\text{Year 5 cost: } 34 \times \$25,000 \times (1.03)^4 = \$382,673$$

Cost calculations continue through Year 23

$$\text{Total Cost} = \$10,147,502$$

²⁸ Number rounds to next closest integer number. Actual value is 34.2