| Type           | Infection                      | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Total |
|----------------|--------------------------------|---------|---------|---------|---------|-------|
| **Bacterial**  |                                |         |         |         |         |       |
|                | enterobacteriaceae             | 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 1 (2.6%)|
|                | enterococcus faecium           | 0 (0.0%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 1 (2.6%)|
|                | escherichia coli               | 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 1 (2.6%)|
|                | MRSA                           | 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 1 (2.6%)|
|                | clostridium difficile          | 0 (0.0%)| 3 (7.9%)| 0 (0.0%)| 0 (0.0%)| 3 (7.9%)|
|                | coagulase negative staphylococcus| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 1 (2.6%)|
|                | enterococcus faecalis          | 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 1 (2.6%)|
|                | pseudomonas aeruginosa         | 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)|
|                | staphylococcus epidermidis     | 0 (0.0%)| 1 (2.6%)| 1 (2.6%)| 0 (0.0%)| 2 (5.3%)|
|                | streptococcus pneumoniae       | 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 1 (2.6%)|
| **Fungal**     |                                |         |         |         |         |       |
|                | aspergillus niger              | 0 (0.0%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 1 (2.6%)|
|                | penicillium                    | 0 (0.0%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 1 (2.6%)|
|                | candida                        | 1 (2.6%)| 2 (5.3%)| 2 (2.6%)| 0 (0.0%)| 5 (13.2%)|
|                | rhizopus                       | 0 (0.0%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 1 (2.6%)|
| **Viral**      |                                |         |         |         |         |       |
|                | BK virus                       | 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 1 (2.6%)|
|                | CMV                            | 0 (0.0%)| 1 (2.6%)| 1 (2.6%)| 0 (0.0%)| 2 (5.3%)|
|                | coronavirus                    | 1 (2.6%)| 2 (5.3%)| 0 (0.0%)| 0 (0.0%)| 3 (7.9%)|
|                | influenza B                    | 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)|
|                | metapneumovirus                | 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 1 (2.6%)| 2 (5.3%)|
|                | norovirus                      | 0 (0.0%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)| 1 (2.6%)|
|                | parainfluenza                  | 0 (0.0%)| 0 (0.0%)| 3 (7.9%)| 1 (2.6%)| 4 (10.5%)|
|                | RSV                            | 0 (0.0%)| 2 (5.3%)| 0 (0.0%)| 0 (0.0%)| 2 (5.3%)|
|                | rhinovirus                     | 0 (0.0%)| 9 (23.7%)| 1 (2.6%)| 0 (0.0%)| 10 (26.3%)|
| **Cryptogenic**|                                |         |         |         |         |       |
|                | cellulitis                     | 0 (0.0%)| 1 (2.6%)| 4 (10.5%)| 0 (0.0%)| 5 (13.2%)|
|                | folliculitis (no organism identified) | 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)|
|                | pneumonia (no organism identified) | 0 (0.0%)| 0 (0.0%)| 2 (5.3%)| 0 (0.0%)| 2 (5.3%)|
|                | sinusitis (no organism identified) | 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)|
|                | skin infection                 | 1 (2.6%)| 0 (0.0%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)|
|                | surgical site infection        | 1 (2.6%)| 0 (0.0%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)|
|                | unidentified organism           | 0 (0.0%)| 1 (2.6%)| 0 (0.0%)| 0 (0.0%)| 1 (2.6%)|
|                | urinary tract infection        | 0 (0.0%)| 1 (2.6%)| 1 (2.6%)| 0 (0.0%)| 2 (5.3%)|

Note: CMV, cytomegalovirus; RSV, respiratory syncytial virus; MRSA, methicillin resistant staphylococcus aureus
### Supplemental Table S2. Comparison of trial results with primary historic and more contemporaneous cGVHD benchmark estimates

| Reference        | Endpoints | Timepoint | Benchmark | Current trial | p-value* |
|------------------|-----------|-----------|-----------|---------------|----------|
|                  |           |           |           | Point estimate | Lower limit of one-sided 90% CI/two-sided 95% CI |         |
| Current trial    | ORR       | 6 months  | 60%       | 62.5%         | 51.5%    | 0.35     |
| BMT CTN 0801     | ORR       | 6 months  | 48.6%     | 62.5%         | 51.5%    | 0.056    |
| Inamoto, 2014    | FFS**     | 12 months | 54%       | 53.1%         | 35.8% - 67.7% | 0.91    |
| Martin, 2017     | FFS (CR/PR)| 12 months| 15%       | 33.5%         | 18.9% - 48.8% | 0.019   |

Note: **after 1st line of cGVHD therapy; ORR, overall response rate; FFS, failure-free survival; CR, complete response; PR, partial response; CI, confidence interval; †Atkinson-Brown estimate; *p-value for FFS and FFS with CR/PR was two-sided and computed by normal approximation at 12 months with standard error estimated by the Greenwood’s approach.
Supplemental Table S3: Association of baseline chronic GVHD features with 6 month clinician-reported ORR

| Baseline variables | Response | Total | p-value |
|--------------------|----------|-------|---------|
|                    | CR+PR (n=20) | Non-response (n=12) | |
| cGVHD type         |           |       |         |
| de novo            | 3 | 15% | 2 | 16.7% | 5 | 0.98 |
| interrupted        | 15 | 75% | 9 | 75% | 24 | |
| progressive        | 2 | 10% | 1 | 8.3% | 3 | |
| Overlap            |           |       |         |
| classic            | 5 | 25% | 4 | 33.3% | 9 | 0.61 |
| overlap            | 15 | 75% | 8 | 66.7% | 23 | |
| IST                |           |       |         |
| 1                  | 11 | 55% | 7 | 58.3% | 18 | 0.45 |
| 2 or 3             | 8 | 40% | 3 | 25% | 11 | |
| N/A                | 1 | 5% | 2 | 16.7% | 3 | |
| Skin               |           |       |         |
| 0                  | 5 | 25% | 2 | 16.7% | 7 | 0.58 |
| >0                 | 15 | 75% | 10 | 83.3% | 25 | |
| 1                  | 2 | 10% | 1 | 8.3% | 3 | 0.29 |
| 2                  | 10 | 50% | 4 | 33.3% | 14 | |
| 3                  | 3 | 15% | 5 | 41.7% | 8 | |
| Mouth              |           |       |         |
| 0                  | 7 | 35% | 4 | 33.3% | 11 | 0.92 |
| >0                 | 13 | 65% | 8 | 66.7% | 21 | |
| 1                  | 9 | 45% | 7 | 58.3% | 16 | 0.34 |
| 2                  | 4 | 20% | 1 | 8.3% | 5 | |
| Eye                |           |       |         |
| 0                  | 4 | 20% | 5 | 41.7% | 9 | 0.19 |
| >0                 | 16 | 80% | 7 | 58.3% | 23 | |
| 1                  | 14 | 70% | 5 | 41.7% | 19 | 0.35 |
| 2                  | 2 | 10% | 2 | 16.7% | 4 | |
| Lung               |           |       |         |
| 0                  | 15 | 75% | 11 | 91.7% | 26 | 0.24 |
| >0                 | 5 | 25% | 1 | 8.3% | 6 | |
| 1                  | 4 | 20% | 1 | 8.3% | 5 | 0.62 |
| 2                  | 1 | 5% | 0 | 0% | 1 | |
| GI                 |           |       |         |
| 0                  | 9 | 45% | 9 | 75% | 18 | 0.098 |
| >0                 | 11 | 55% | 3 | 25% | 14 | |
|                | 0  | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  |
|----------------|----|----|----|----|----|----|----|----|----|
| **Liver**      | 0  | 10 | 6  | 16 | 16 | 1  |
| >0             | 10 | 50%| 6  | 50%| 16 | 1  |
| 1              | 4  | 20%| 5  | 41.7%| 9  | 0.19|
| 2              | 3  | 15%| 0  | 0%  | 3  |
| 3              | 3  | 15%| 1  | 8.3%| 4  |
| **Genital**    | 0  | 17 | 12 | 29 | 29 | 0.16|
| >0             | 3  | 15%| 0  | 0%  | 3  |
| 1              | 2  | 10%| 0  | 0%  | 2  |
| 2              | 1  | 5% | 0  | 0%  | 1  |
| **Joint/fascia**| 0  | 8  | 6  | 14 | 14 | 0.58|
| >0             | 12 | 60%| 6  | 50%| 18 | 0.50|
| 1              | 6  | 30%| 4  | 33.3%| 10 | 0.50|
| 2              | 6  | 30%| 2  | 16.7%| 8  |
| **Overall severity** | moderate | 13 | 65%| 6  | 50%| 19 | 0.40|
| severe         | 7  | 35%| 6  | 50%| 13 |     |

* CR – complete response, PR – partial response, non-response – (SD, stable disease + PD, progressive disease), cGVHD – chronic graft vs. host disease, IST – immune suppressive therapy
Supplemental Table S4: Durability of 6 month clinician-reported ORR per subsequent response assessments

| Ongoing Response at each month | 9 month | 12 month | 18 month | 24 month |
|-------------------------------|---------|----------|----------|----------|
|                               | n       | %        | n        | %        | n        | %        | n        | %        |
| Failure (SD + PD)             | 6 30%   | 9 45%    | 14 70%   | 15 75%   |
| Response (CR+PR)              | 14 70%  | 11 55%   | 6 30%    | 5 25%    |
| Total                         | 20 20%  | 20 20%   | 20 20%   | 20 20%   |

Note: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease
### Supplemental Table S5: NIH 0-3 score change over time per involved organ sites

| Organ | Score | Baseline | | | | | | | Time |
|-------|-------|----------|----------|----------|----------|----------|----------|----------|-----------------=|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|       |       | n       | %       | n       | %       | n       | %       | n       | %       | n       | %       | n       | %       | n       | %       | n       | %       |
| Skin  |       |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
|       | 0     | 9       | 23.7%   | 15      | 44.1%   | 17      | 53.1%   | 15      | 57.7%   | 12      | 50.0%   | 10      | 47.6%   | 10      | 50%   |         |
|       | 1     | 4       | 10.5%   | 4       | 11.8%   | 7       | 21.9%   | 4       | 15.4%   | 2       | 8.3%    | 2       | 9.5%    | 2       | 10%   |         |
|       | 2     | 16      | 42.1%   | 11      | 32.4%   | 4       | 12.5%   | 3       | 11.5%   | 6       | 25.0%   | 5       | 23.8%   | 3       | 15%   |         |
|       | 3     | 9       | 23.7%   | 4       | 11.8%   | 4       | 12.5%   | 4       | 15.4%   | 4       | 16.7%   | 4       | 19.0%   | 5       | 25%   |         |
|       | Total | 38      |         | 34      |         | 32      |         | 26      |         | 24      |         | 21      |         | 20      |         |         |         |
| Mouth |       |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
|       | 0     | 11      | 28.9%   | 23      | 67.6%   | 19      | 59.4%   | 20      | 76.9%   | 17      | 70.8%   | 15      | 71.4%   | 18      | 90%   |         |
|       | 1     | 22      | 57.9%   | 10      | 29.4%   | 11      | 34.4%   | 5       | 19.2%   | 5       | 20.8%   | 5       | 23.8%   | 1       | 5%    |         |
|       | 2     | 5       | 13.2%   | 0       | 0.0%    | 2       | 6.3%    | 1       | 3.8%    | 1       | 4.2%    | 1       | 4.8%    | 1       | 5%    |         |
|       | 3     | 0       | 0.0%    | 1       | 2.9%    | 0       | 0.0%    | 0       | 0.0%    | 1       | 4.2%    | 0       | 0.0%    | 0       | 0%    |         |
|       | Total | 38      |         | 34      |         | 32      |         | 26      |         | 24      |         | 21      |         | 20      |         |         |         |
| Eye   |       |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
|       | 0     | 12      | 31.6%   | 12      | 35.3%   | 13      | 40.6%   | 10      | 38.5%   | 5       | 20.8%   | 5       | 23.8%   | 7       | 35%   |         |
|       | 1     | 20      | 52.6%   | 17      | 50.0%   | 12      | 37.5%   | 9       | 34.6%   | 12      | 50.0%   | 12      | 57.1%   | 9       | 45%   |         |
|       | 2     | 6       | 15.8%   | 5       | 14.7%   | 7       | 21.9%   | 7       | 26.9%   | 5       | 20.8%   | 3       | 14.3%   | 4       | 20%   |         |
|       | 3     | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 2       | 8.3%    | 1       | 4.8%    | 0       | 0%    |         |
|       | Total | 38      |         | 34      |         | 32      |         | 26      |         | 24      |         | 21      |         | 20      |         |         |         |
| Lung  |       |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
|       | 0     | 30      | 78.9%   | 30      | 88.2%   | 28      | 87.5%   | 22      | 84.6%   | 21      | 87.5%   | 18      | 85.7%   | 17      | 85%   |         |
|       | 1     | 7       | 18.4%   | 4       | 11.8%   | 3       | 9.4%    | 4       | 15.4%   | 3       | 12.5%   | 3       | 14.3%   | 1       | 5%    |         |
|       | 2     | 1       | 2.6%    | 0       | 0.0%    | 1       | 3.1%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 2       | 10%   |         |
|       | 3     | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0%    |         |
|       | Total | 38      |         | 34      |         | 32      |         | 26      |         | 24      |         | 21      |         | 20      |         |         |         |
| GI    |       |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
|       | 0     | 21      | 55.3%   | 31      | 91.2%   | 29      | 90.6%   | 22      | 84.6%   | 21      | 87.5%   | 18      | 85.7%   | 19      | 95%   |         |
|       | 1     | 13      | 34.2%   | 2       | 5.9%    | 3       | 9.4%    | 4       | 15.4%   | 3       | 12.5%   | 3       | 14.3%   | 1       | 5%    |         |
|       | 2     | 4       | 10.5%   | 1       | 2.9%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0%    |         |
|       | 3     | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0.0%    | 0       | 0%    |         |
|       | Total | 38      |         | 34      |         | 32      |         | 26      |         | 24      |         | 21      |         | 20      |         |         |         |
| Liver |       |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
|       | 0     | 19      | 50.0%   | 21      | 61.8%   | 21      | 65.6%   | 22      | 84.6%   | 17      | 70.8%   | 16      | 88.9%   | 11      | 78.6% |         |
|       | 1     | 12      | 31.6%   | 10      | 29.4%   | 6       | 18.8%   | 4       | 15.4%   | 5       | 20.8%   | 1       | 5.6%    | 1       | 7.1%  |         |
| Organ     | Score | Baseline n | Baseline % | Month 3 n | Month 3 % | Month 6 n | Month 6 % | Month 9 n | Month 9 % | Month 12 n | Month 12 % | Month 18 n | Month 18 % | Month 24 n | Month 24 % |
|-----------|-------|------------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Genital   | 2     | 3          | 7.9%       | 3         | 8.8%      | 5         | 15.6%     | 0         | 0.0%      | 2         | 8.3%      | 1         | 5.6%      | 2         | 14.3%     |
|           | 3     | 4          | 10.5%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      |
| Total     |       | 38         | 34         | 32        | 26        | 24        | 18        | 14        |           |           |           |           |           |           |           |
| Genital   | 0     | 35         | 92.1%      | 33        | 97.1%     | 30        | 93.8%     | 24        | 92.3%     | 22        | 91.7%     | 18        | 90.0%     | 14        | 93.3%     |
|           | 1     | 2          | 5.3%       | 1         | 2.9%      | 1         | 3.1%      | 2         | 7.7%      | 2         | 8.3%      | 1         | 5.0%      | 1         | 6.7%      |
|           | 2     | 1          | 2.6%       | 0         | 0.0%      | 1         | 3.1%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      |
|           | 3     | 0          | 0.0%       | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 1         | 5.0%      | 0         | 0.0%      |
| Total     |       | 38         | 34         | 32        | 26        | 24        | 20        | 15        |           |           |           |           |           |           |           |
| Joint/fascia | 0    | 18         | 47.4%      | 20        | 58.8%     | 22        | 68.8%     | 16        | 61.5%     | 17        | 70.8%     | 11        | 52.4%     | 10        | 50%       |
|           | 1     | 11         | 28.9%      | 13        | 38.2%     | 9         | 28.1%     | 9         | 34.6%     | 7         | 29.2%     | 8         | 38.1%     | 7         | 35%       |
|           | 2     | 9          | 23.7%      | 1         | 2.9%      | 1         | 3.1%      | 1         | 3.8%      | 0         | 0.0%      | 2         | 9.5%      | 3         | 15%       |
|           | 3     | 0          | 0.0%       | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0.0%      | 0         | 0%        |
| Total     |       | 38         | 34         | 32        | 26        | 24        | 21        | 20        |           |           |           |           |           |           |           |
# Supplemental Table S6: Serial evaluation of grip strength and 2 minute walk test according to clinician-reported 6 month response (CR/PR as responder vs. others as non-responder)

|                  | Responders (n=20) | Non-responders (n=12) | p-value |
|------------------|-------------------|-----------------------|---------|
|                  | n |
| **Grip**         |    |
| Baseline         | 20 |
| 2 weeks          | 19 |
| 1 month          | 18 |
| 3 months         | 14 |
| 6 months         | 15 |
| 9 months         | 10 |
| 12 months        | 7  |
| 18 months        | 4  |
| 24 months        | 4  |
|                  | Mean (SD) | Median (Range) | Mean (SD) | Median (Range) |
| Baseline         | 49.1 (24.7) | 49.5 (13.6 – 94) | 51.2 (20.1) | 53.3 (27.6 – 97) |
| 2 weeks          | 53.6 (23)  | 52 (18.3 – 96)     | 55.6 (21.3) | 57 (23 – 90.3)  |
| 1 month          | 55.8 (23.7)| 62.5 (19 – 102)    | 54.4 (21.9) | 56 (20.3 – 101) |
| 3 months         | 50.9 (25.9)| 46.3 (15 – 98)     | 59.1 (22.9) | 60 (21 – 105.7) |
| 6 months         | 60.7 (23.4)| 59 (15 – 104)      | 65.4 (19.6) | 64 (34 – 93)    |
| 9 months         | 66.6 (28.7)| 69.5 (32 – 117)    | 65.9 (16.1) | 60 (50 – 96)    |
| 12 months        | 68.2 (19.9)| 74 (38 – 92)       | 68.6 (23.1) | 62.5 (35.3 – 104.6) |
| 18 months        | 66.3 (22.3)| 74.9 (33.3 – 82)   | 62.4 (30.9) | 54.5 (28.6 – 109.3) |
| 24 months        | 62.9 (14.3)| 68 (42 – 73.7)     | 46.5 (12)  | 46.5 (38 – 55)  |
| **Walk**         |    |
| Baseline         | 424.7 (111.5)| 410.5 (265 – 628) | 453.4 (85.9) | 442 (300 – 561) |
| 2 weeks          | 436.8 (125.3)| 441 (200 – 626)   | 515.2 (87.6) | 525 (400 – 700) |
| 1 month          | 457.7 (119.6)| 500 (250 – 651)   | 507.1 (79)  | 501 (384 – 595) |
| 3 months         | 420.2 (125.7)| 450 (250 – 588)   | 516.4 (97.9) | 534 (362 – 652) |
| 6 months         | 482.7 (92.9)| 500 (300 – 643)   | 496 (99.3)  | 466 (403 – 643) |
| 9 months         | 516 (130.2)| 527 (300 – 750)   | 496.6 (164.6)| 486 (312 – 678) |
| 12 months        | 499.8 (147.4)| 504 (228 – 633)   | 485.4 (130) | 461 (312 – 692) |
| 18 months        | 498.3 (120.1)| 487 (392 – 627)   | 505.3 (129.5)| 465 (358 – 674) |
| 24 months        | 465 (139.7)| 500 (274 – 586)   | 392 (NA)    | 392 (NA)         |

* A mixed effect model was used to evaluate the difference in slope between responders and non-responders. Up to 24 months, no significant difference in trend between responders and non-responders was observed (p-values for Grip and Walk are 0.94 and 0.78, respectively). Up to 6 months, no significant difference in trend between responders and non-responders was observed (p-values for Grip and Walk are 0.94 and 0.83, respectively).
### Supplemental Table S7: Additional lines of subsequent systemic immunosuppressive therapy beyond the study intervention

| Lines of therapy | Moffitt (N=24) | FHCRC (N=9) | UMN (N=5) | Total (N=38) |
|------------------|----------------|-------------|-----------|--------------|
| IS beyond prednisone #1 |                |             |           |              |
| ECP              | 2 8.3%         | 1 11.1%     | 0 0%      | 3 7.9%       |
| MMF              | 2 8.3%         | 1 11.1%     | 0 0%      | 3 7.9%       |
| MTX              | 1 4.2%         | 0 0%        | 0 0%      | 1 2.6%       |
| tacrolimus       | 2 8.3%         | 0 0%        | 0 0%      | 1 2.6%       |
| ibrutinib        | 0 0%           | 1 11.1%     | 0 0%      | 1 2.6%       |
| ruxolitinib      | 1 4.2%         | 0 0%        | 0 0%      | 1 2.6%       |
| sirolimus        | 0 0%           | 2 22.2%     | 0 0%      | 2 5.3%       |
| none             | 16 66.7%       | 4 44.4%     | 5 100%    | 25 65.8%     |
| IS beyond prednisone #2 |            |             |           |              |
| ECP              | 2 8.3%         | 0 0%        | 0 0%      | 2 5.3%       |
| KD025            | 0 0%           | 1 11.1%     | 0 0%      | 1 2.6%       |
| MMF              | 0 0%           | 2 22.2%     | 0 0%      | 2 5.3%       |
| PUVA             | 0 0%           | 1 11.1%     | 0 0%      | 1 2.6%       |
| ibrutinib        | 0 0%           | 1 11.1%     | 0 0%      | 1 2.6%       |
| pentostatin      | 1 4.2%         | 0 0%        | 0 0%      | 1 2.6%       |
| ruxolitinib      | 1 4.2%         | 0 0%        | 0 0%      | 1 2.6%       |
| sirolimus        | 1 4.2%         | 0 0%        | 0 0%      | 1 2.6%       |
| none             | 19 79.2%       | 4 44.4%     | 5 100%    | 28 73.7%     |
| IS beyond prednisone #3 |            |             |           |              |
| ECP              | 1 4.2%         | 2 22.2%     | 0 0%      | 3 7.9%       |
| methotrexate     | 0 0%           | 1 11.1%     | 0 0%      | 1 2.6%       |
| ruxolitinib      | 0 0%           | 1 11.1%     | 0 0%      | 1 2.6%       |
| none             | 23 95.8%       | 5 55.6%     | 5 100%    | 33 86.8%     |
| IS beyond prednisone #4 |            |             |           |              |
| ECP              | 0 0%           | 1 11.1%     | 0 0%      | 1 2.6%       |
| ibrutinib        | 1 4.2%         | 0 0%        | 0 0%      | 1 2.6%       |
| none             | 23 95.8%       | 8 88.9%     | 5 100%    | 36 94.7%     |
| IS beyond prednisone #5 |            |             |           |              |
| KD025            | 0 0%           | 1 11.1%     | 0 0%      | 1 2.6%       |
| none             | 24 100%        | 8 88.9%     | 5 100%    | 37 97.4%     |

Note: Numbered agents (e.g. IS beyond prednisone #1) indicate the numbered sequential lines of systemic IS therapy given after prednisone/ofatumumab; FHCRC, Fred Hutchinson Cancer Research Center; UMN, University of Minnesota; ECP, extra-corporeal photopheresis; MMF, mycophenolate mofetil; MTX, methotrexate; PUVA, psoralen-UVA ultraviolet light therapy; KD025, belumosudil
Supplemental Table S8: Immune reconstitution in subset of Moffitt participants

(a) Immune cell populations

| Immune cell type | Time     | Moffitt Subjects (n=24) |   |   |
|------------------|----------|-------------------------|---|---|
|                  |          | N  | Mean (SD) | Median (Range) |   |   |
| CD45, absolute   | Baseline | 23 | 1.28 (1.12) | 0.78 (0.08 - 3.96) |   |   |
|                  | Day 14   | 2  | 0.22 (0.17) | 0.22 (0.1 - 0.34) |   |   |
|                  | Month 3  | 19 | 1.14 (0.90) | 1 (0.27 - 4.18) |   |   |
|                  | Month 6  | 19 | 1.48 (1.27) | 1.09 (0.36 - 4.56) |   |   |
|                  | Month 12 | 15 | 1.38 (0.66) | 1.36 (0.21 - 2.56) |   |   |
| CD3              | Baseline | 23 | 0.86 (0.82) | 0.6 (0.03 - 3.24) |   |   |
|                  | Day 14   | 2  | 0.17 (0.18) | 0.17 (0.05 - 0.30) |   |   |
|                  | Month 3  | 19 | 1 (0.93)    | 0.79 (0.15 - 4.10) |   |   |
|                  | Month 6  | 19 | 1.29 (1.18) | 1.04 (0.11 - 3.99) |   |   |
|                  | Month 12 | 15 | 1.15 (0.59) | 1.03 (0.16 - 2.37) |   |   |
| CD4              | Baseline | 23 | 0.33 (0.24) | 0.29 (0.02 - 0.93) |   |   |
|                  | Day 14   | 2  | 0.07 (0.06) | 0.07 (0.03 - 0.11) |   |   |
|                  | Month 3  | 19 | 0.43 (0.34) | 0.32 (0.08 - 1.24) |   |   |
|                  | Month 6  | 19 | 0.54 (0.45) | 0.37 (0.08 - 1.4)  |   |   |
|                  | Month 12 | 15 | 0.59 (0.32) | 0.54 (0.04 - 1.45) |   |   |
| CD8              | Baseline | 23 | 0.51 (0.64) | 0.24 (0.02 - 2.7)  |   |   |
|                  | Day 14   | 2  | 0.11 (0.12) | 0.11 (0.02 - 0.19) |   |   |
|                  | Month 3  | 19 | 0.56 (0.69) | 0.38 (0.05 - 3.13) |   |   |
|                  | Month 6  | 19 | 0.73 (0.79) | 0.38 (0.04 - 2.64) |   |   |
|                  | Month 12 | 15 | 0.55 (0.41) | 0.5 (0.12 - 1.64)  |   |   |
| CD16CD56         | Baseline | 23 | 0.12 (0.09) | 0.1 (0.01 - 0.36)  |   |   |
|                  | Day 14   | 2  | 0.04 (0.02) | 0.04 (0.03 - 0.05) |   |   |
|                  | Month 3  | 19 | 0.12 (0.06) | 0.12 (0.04 - 0.26) |   |   |
|                  | Month 6  | 19 | 0.17 (0.12) | 0.16 (0.04 - 0.49) |   |   |
|                  | Month 12 | 15 | 0.16 (0.09) | 0.14 (0.04 - 0.32) |   |   |
| CD19             | Baseline | 23 | 0.30 (0.44) | 0.12 (0 - 1.59)   |   |   |
|                  | Day 14   | 2  | 0 (0)        | 0 (0)               |   |   |
|                  | Month 3  | 19 | 0 (0.001)   | 0 (0 - 0.002)       |   |   |
|                  | Month 6  | 19 | 0 (0.001)   | 0 (0 - 0.004)       |   |   |
### Immune cell type

| Time       | CD4/CD8 | Moffitt Subjects (n=24) | | | | | | | |
|------------|---------|-------------------------|---|---|---|---|
|            | N       | Mean (SD)               | Median (Range) | | | | | | |
| Month 12   | 15      | 0.03 (0.05)             | 0.002 (0 - 0.17) | | | | | | |
| Baseline   | 24      | 1.32 (1.04)             | 0.93 (0.19 - 4.28) | | | | | | |
| Day 14     | 2       | 1.03 (0.66)             | 1.03 (0.56 - 1.49) | | | | | | |
| Month 3    | 19      | 1.21 (0.81)             | 0.97 (0.33 - 3.11) | | | | | | |
| Month 6    | 19      | 1.15 (0.76)             | 0.97 (0.21 - 2.7)  | | | | | | |
| Month 12   | 15      | 1.4 (0.89)              | 1.14 (0.33 - 3.04) | | | | | | |

### Quantitative immunoglobulins

| Ig Cell Type | Time       | n   | Moffitt Subjects (n=24) | | | | | | |
|--------------|------------|-----|-------------------------|---|---|---|---|
|              |            |     | N                       | Mean (SD) | Median (Range) | | | | | |
| IgG          | Baseline   | 22  | 753.14 (594.15)         | 650.5 (0 - 2765) | | | | | | |
|              | Day 14     | 2   | 464 (189.5)             | 464 (330 - 598) | | | | | | |
|              | Month 3    | 17  | 405.24 (256.05)         | 470 (0 - 800) | | | | | | |
|              | Month 6    | 14  | 349.21 (247.28)         | 405.5 (0 - 663) | | | | | | |
|              | Month 12   | 15  | 399.27 (190.63)         | 427 (0 - 700) | | | | | | |
| IgA          | Baseline   | 22  | 93.59 (76.79)           | 99.5 (0 - 292) | | | | | | |
|              | Day 14     | 1   | 86 (NA)                 | 86 (NA) | | | | | | |
|              | Month 3    | 17  | 73.94 (61.1)            | 81 (0 - 219) | | | | | | |
|              | Month 6    | 14  | 63.79 (60.95)           | 71.5 (0 - 215) | | | | | | |
|              | Month 12   | 14  | 80.21 (89.66)           | 77 (0 - 319) | | | | | | |
| IgM          | Baseline   | 22  | 94.14 (127.11)          | 53.5 (0 - 562) | | | | | | |
|              | Day 14     | 1   | 0 (NA)                  | 0 (NA) | | | | | | |
|              | Month 3    | 17  | 26.35 (24.06)           | 31 (0 - 86) | | | | | | |
|              | Month 6    | 14  | 18.71 (21.09)           | 13.5 (0 - 61) | | | | | | |
|              | Month 12   | 14  | 13.57 (19.29)           | 0 (0 - 47) | | | | | | |
| IgE          | Baseline   | 22  | 152.14 (346.67)         | 12.5 (0 - 1474) | | | | | | |
|              | Day 14     | 0   | NA                      | NA | | | | | | |
|              | Month 3    | 17  | 31.71 (55.41)           | 6 (0 - 199) | | | | | | |
|              | Month 6    | 14  | 34.64 (69.55)           | 5.5 (0 - 236) | | | | | | |
|              | Month 12   | 14  | 40.79 (100.65)          | 4.5 (0 - 373) | | | | | | |
Supplemental Table S9: Infection density and association with prednisone exposure and quantitative immunoglobulins

(a) Infection density per follow up time frames

| Time          | N, infections | Follow-up, patient days | Infection density |
|---------------|---------------|-------------------------|-------------------|
| All Subjects  | at Day 30     | 7                       | 1131              | 6.19              |
|               | Day 31 - 180 | 31                      | 5029              | 6.16              |
|               | Day 181 - 365| 13                      | 5670              | 2.29              |

(b) Descriptive data on cumulative prednisone dose and quantitative immunoglobulins

| Variables          | Time Point | N  | Mean  | SD   | Median | Min  | Max  |
|--------------------|------------|----|-------|------|--------|------|------|
| Prednisone, cumulative* | at Day 30  | 37 | 19.53 | 5.42 | 20.11  | 10.69| 28.94|
|                    | at Day 180 | 31 | 53.83 | 20.55| 58.24  | 16.84| 89.71|
|                    | at Day 365 | 29 | 74.44 | 34.36| 72.93  | 18.80| 147.07|
| Average IgG        | Baseline   | 22 | 753.14| 594.15| 650.50 | 0    | 2765.00|
|                    | at Day 30  | 17 | 616.50| 426.13| 551.50 | 0    | 1782.50|
|                    | at Day 180 | 14 | 465.36| 321.51| 493.63 | 0    | 1257.00|
|                    | at Day 365 | 15 | 443.13| 250.11| 463.13 | 0    | 969.25|
| Average IgA        | Baseline   | 22 | 93.59 | 76.79| 99.50  | 0    | 292.00|
|                    | at Day 30  | 17 | 87.15 | 67.61| 98.00  | 0    | 224.00|
|                    | at Day 180 | 14 | 68.63 | 60.75| 85.88  | 0    | 210.50|
|                    | at Day 365 | 14 | 80.58 | 53.65| 82.69  | 0    | 160.25|
| Average IgM        | Baseline   | 22 | 94.14 | 127.11| 53.50  | 0    | 562.00|
|                    | at Day 30  | 17 | 52.29 | 46.90| 44.00  | 0    | 183.00|
|                    | at Day 180 | 14 | 48.05 | 76.69| 36.63  | 0    | 297.00|
|                    | at Day 365 | 14 | 22.34 | 18.59| 27.75  | 0    | 53.38|
| Average IgE        | Baseline   | 22 | 152.14| 346.67| 12.50  | 0    | 1474.00|
|                    | at Day 30  | 17 | 69.06 | 128.14| 9.50   | 0    | 509.50|
|                    | at Day 180 | 14 | 103.00| 234.97| 5.75   | 0    | 855.00|
|                    | at Day 365 | 14 | 59.13 | 138.95| 5.38   | 0    | 516.75|

*normalized cumulative prednisone dose (average daily prednisone dose/kg x days)
### (c) Infection density through day 30 and association with prednisone dose and immunoglobulin levels

| Variables                  | N | N, infections | Follow-up, patient days | Infection density | p-value |
|----------------------------|---|---------------|-------------------------|-------------------|---------|
| Prednisone, cumulative     |   |              |                         |                   |         |
| at Day 30                  | ≤ Median | 19 | 3 | 570 | 5.26 | 0.65 |
|                           | > Median | 18 | 4 | 540 | 7.41 |       |
| IgG                       |   |              |                         |                   |         |
| Baseline                  | ≤ Median | 11 | 4 | 330 | 12.12 | 0.045 |
|                           | > Median | 11 | 0 | 330 | 0.00 |       |
| IgA                       |   |              |                         |                   |         |
| Baseline                  | ≤ Median | 11 | 4 | 330 | 12.12 | 0.045 |
|                           | > Median | 11 | 0 | 330 | 0.00 |       |
| IgM                       |   |              |                         |                   |         |
| Baseline                  | ≤ Median | 11 | 2 | 330 | 6.06 | >0.99 |
|                           | > Median | 11 | 2 | 330 | 6.06 |       |
| IgE                       |   |              |                         |                   |         |
| Baseline                  | ≤ Median | 11 | 4 | 330 | 12.12 | 0.045 |
|                           | > Median | 11 | 0 | 330 | 0.00 |       |

### (d) Infection density day 31-180 and association with prednisone dose and immunoglobulin levels

| Variables                  | N | N, infections | Follow-up, patient days | Infection density | p-value |
|----------------------------|---|---------------|-------------------------|-------------------|---------|
| Prednisone, cumulative     |   |              |                         |                   |         |
| at Day 180                 | ≤ Median | 16 | 6 | 2400 | 2.50 | 0.18 |
|                           | > Median | 15 | 11 | 2250 | 4.89 |       |
| IgG                       |   |              |                         |                   |         |
| at Day 180                 | ≤ Median | 7 | 1 | 1050 | 0.95 | 0.18 |
|                           | > Median | 7 | 4 | 1050 | 3.81 |       |
| IgA                       |   |              |                         |                   |         |
| at Day 180                 | ≤ Median | 7 | 1 | 1050 | 0.95 | 0.18 |
|                           | > Median | 7 | 4 | 1050 | 3.81 |       |
| IgM                       |   |              |                         |                   |         |
| at Day 180                 | ≤ Median | 7 | 3 | 1050 | 2.86 | 0.65 |
|                           | > Median | 7 | 2 | 1050 | 1.90 |       |
| IgE                       |   |              |                         |                   |         |
| at Day 180                 | ≤ Median | 7 | 3 | 1050 | 2.86 | 0.65 |
|                           | > Median | 7 | 2 | 1050 | 1.90 |       |
(e) Infection density day 181-365 and association with prednisone dose and immunoglobulin levels

| Variables            | at Day 365 | N ≤ Median | N infections | Follow-up, patient days | Infection density | p-value |
|----------------------|------------|------------|--------------|------------------------|-------------------|---------|
| Prednisone, cumulative |            | 15         | 3            | 2730                   | 1.10              | 0.18    |
|                      |            | 14         | 7            | 2590                   | 2.70              |         |
| IgG                  |            | 7          | 2            | 1480                   | 1.35              | 0.89    |
|                      |            | 7          | 2            | 1295                   | 1.54              |         |
| IgA                  |            | 7          | 2            | 1295                   | 1.54              | >0.99   |
|                      |            | 7          | 2            | 1295                   | 1.54              |         |
| IgM                  |            | 7          | 2            | 1295                   | 1.54              | >0.99   |
|                      |            | 7          | 2            | 1295                   | 1.54              |         |
| IgE                  |            | 7          | 1            | 1295                   | 0.77              | 0.32    |
|                      |            | 7          | 3            | 1295                   | 2.32              |         |
Supplemental Figure S1: Baseline organ involvement and severity of cGVHD
Supplemental Figure S2: Longitudinal trends in immune cell subsets and quantitative immunoglobulins

(a) Immune cell populations (total lymphocytes, CD3, CD4, CD8, NK, and total B cells) for n=24 subjects
(b) Quantitative immunoglobulins (IgG, IgA, IgM, IgE) for n=24 subjects
Supplemental Figure S3: Prednisone dose taper over time on study