

Best of ASCO 2017

SCO 2017 was filled with new information and long lines as 39,000 oncologists worldwide came together to hear the latest advances in cancer care. The quality of research and originality of studies, however, made any inconvenience worthwhile. Here are my thoughts about the best of ASCO 2017.

Practice Management Issues

At the pre-ASCO session on Economics of Cancer Care, presentations focused on the OCM, MIPS, and drug pricing. Every oncology practice is now impacted by either MACRA, MIPS, or alternative payment models, which started in January 2017. Because of the compliance-related frustration of reporting in the OCM, networking with other participants is necessary, and attending meetings at ASCO, ACCC, and other venues is strongly recommended. The best tip was to stress coordination among physicians, nurses, and advanced practitioners, as well as specialists and supportive care services.

Another issue of importance is value. There is not agreement on the elements of value, and this is evident in the comparisons of ASCO (version 1 and version 2), ESMO, NCCN, ICER, and others. S. Cheng and coauthors (Abstract 6509) described the very poor correlation coefficient values for each of the frameworks (ASCO1, ASCO2, and ESMO) and the poor agreement between the frameworks and ultimate decisions by the payers NICE and pCODR.

ACRONYM LEGEND

ACA: Affordable Care Act ADT: Androgen deprivation therapy ALL: Acute lymphocytic leukemia AML: Acute myelocytic leukemia CBR: Clinical benefit rate (CR+PR+SD) CNS: Central nervous system CR: Complete response DFS: Disease-free survival EGFR: Epidermal growth factor ESMO: European Society of Medical Oncology HR: Hazard Ratio ICER: Institute for Clinical and Economic Review **IMiD:** Immunomodulatory drug

LBA: Late breaking abstract

MACRA: Medicare Access and Chip Reauthorization Act

MIPS: Merit-based Incentive Payment System

Mo: Months

NCCN: National Comprehensive Cancer Network

NHL: Non-Hodgkin's lymphoma

NICE: National Institute for Health Care Excellence

NSCLC: Non-small cell lung cancer OCM: Oncology Care Model **OS:** Overall survival **pCODR:** Pan Canadian Oncology Drug Review

PFS: Progression free survival

PR: Partial response

PSA: Prostate-specific antigen

QOL: Quality of life

R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine plus prednisone

R-CVP: Rituximab, cyclophosphamide, vincristine plus prednisone

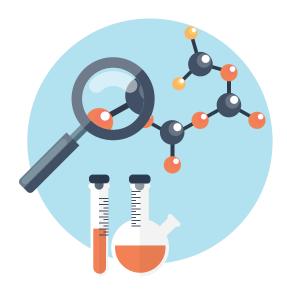
RR: Response rate (CR+PR)

SD: Stable disease

Vs: Versus

Breast Cancer

- In a plenary session, M. Robson and colleagues (Abstract LBA4) presented a Phase III trial of olaparib monotherapy vs treating physician choice of chemotherapy (TPC with capecitabine, eribulin, or vinorelbine) in patients with a germline BRCA mutation with up to 2 lines of prior chemotherapy. PFS was improved in olaparib patients 7.0 mo vs 4.2 mo, HR 0.58 (p=0.0009).
- Abstract LBA500, G. Von Minckwitz and colleagues presented results of the APHINITY trial. Addition of pertuzumab to chemotherapy plus trastuzumab increased invasive DFS from 90.6% to 92.3% at 4 years, HR 0.81 (p=0.045). The improvement: 3.2% in node-positive patients and 2.3% in hormone receptor-negative patients.
- Abstract LBA10066, M. Lambertini et al. showed that in patients with breast cancer, pregnancy did not adversely affect DFS, HR 0.85 (p=0.15). In patients with estrogen receptor negative cancer, pregnancy appeared to improve survival, HR 0.57 (p=0.02). Pregnancy appears safe in all breast cancer patients.
- In the ALTTO trial, A. Moreno-Aspitia et al. (Abstract 502) showed that addition of lapatinib to trastuzumab adjuvant therapy increased the DFS slightly from 82% to 85% at 6 years, HR 0.86.
- R. Nanda et al. (Abstract 506) showed in the I-SPY 2 trial that pembrolizumab improved the pathological CR rate with paclitaxel in triple negative breast cancer patients from 19% to 71%, and in hormone receptor-positive patients from 14% to 28%.
- In patients with isolated locoregional recurrence, I. Wapnir et al. (Abstract 513) showed that for hormone receptor-positive



patients, the addition of chemotherapy to surgery, radiation, and hormonal therapy did not change DFS or OS. However, for hormone receptor-negative patients, 10-year OS with chemotherapy was 73% vs only 53% without, HR 0.48.

- G. Sledge et al. (Abstract 1000) presented the MONARCH 2 trial in endocrine-resistant patients. Abemaciclib plus fulvestrant increased the PFS to 16.4 mo vs fulvestrant alone 9.3 mo, HR 0.55, (p<000001). RR was increased to 48% from 2%.
- R. Finn and colleagues (Abstract 1001), however, reported that in the PALOMA-1 trial the OS of letrozole was 34.5 mo and only increased to 37.5 mo with addition of palbociclib (p=0.28 not significant).
- Abstract 1002, L. Malorni et al. showed that in patients with progression on prior endocrine therapy, addition of palbociclib presented an increase in PFS to 11.5 mo compared to only 6.5 mo with palbociclib alone, HR 0.53 (p=0.02). Palbociclib can reverse resistance.
- E. Perez and colleagues (Abstract 1003) described the MARI-ANNE trial. The less expensive trastuzumab plus docetaxel had the same effect on OS compared to T-DM1 or T-DM1 plus pertuzumab. Duration of response seemed longer on T-DM1, however.
- W. Gradishar et al. (*Abstract 1004*) showed superiority of a non-chemotherapy treatment with lapatinib plus trastuzumab plus aromatase inhibitor, PFS 11 mo vs 5.7 mo without lapatinib (p=0.006) or without trastuzumab 8.3 mo (p=0.04). Patients had prior chemotherapy with trastuzumab.
- In 31 HER2+ breast cancer patients with brain metastases treated with neratinib and capecitabine, R. Freedman and colleagues (*Abstract 1005*) showed a RR of 49% and SD at 6 cycles of 32%, with a median duration of response of 5.5 mo and OS 13.5 mo.
- Abstract 1011, C. Anders and coauthors reported on the treatment of HER2+ breast cancer patients with brain metastases treated with everolimus, trastuzumab, and vinorelbine. There was a CBR at 6 mo of 27% and OS was 12.2 mo.

Colorectal Cancer

In a plenary session presentation, Q. Shi and colleagues (Abstract LBA1) studied a meta-analysis of 3 national adjuvant studies of Stage III and II colon cancer patients. Although overall FOLFOX or XELOX for 3 mo was noninferior to 6 mo of therapy, in patients with stage T4 or N2 disease, 3 mo was inferior to 6 mo of therapy, DFS HR 1.12. Consensus of the discussion suggested that in T1-3 N1 disease, 3 mo of therapy was sufficient and less toxic (17% grade 2 or higher neurotoxicity vs 48% with 6 mo); however, for T4 or N2 patients, 6 mo would be preferable but with consideration of the neurotoxicity.

- F. Innocenti et al. (Abstract 3504) showed the molecular correlates of patients on metastatic disease study CALGB/SWOG 80405 (Alliance) comparing bevacizumab with cetuximab. Patients with MSI-high showed superiority of bevacizumab vs cetuximab OS 30 mo vs 11 mo, HR 0.13 (p=0.0002). In patients with BRAF mutation, bevacizumab was superior to cetuximab, OS 17 mo vs 10 mo, HR 0.49.
- In protocol S1406, S. Kopetz and colleagues (Abstract 3505) showed that in the 7% of colon cancer patients with mutated BRAF in second- or third-line chemotherapy, addition of vemurafenib to irinotecan plus cetuximab increased PFS from 2.0 mo to 4.3 mo, HR 0.48 (p=0.001). OS increased from 5.9 mo to 9.6 mo, HR 0.7 (p=0.19).
- In an interesting study, K. Ng and colleagues (Abstract 3506) showed that in previously untreated metastatic colon cancer patients who were receiving FOLFOX chemotherapy with bevacizumab (the SUNSHINE study), addition of high doses of vitamin D 8000 iu/day for 2 weeks then 4000 iu/day, had superior results compared to low-dose vitamin D 400 iu/day. PFS was longer 13.1 mo vs 11.2 mo, HR 0.69 (p=0.04), and there was less diarrhea (p=0.02).
- Abstract 10006, E. Van Blarigan et al. showed that among localized colorectal cancer patients treated with adjuvant chemotherapy on CALGB protocol 89803 (Alliance), patients who complied with American Cancer Society guidelines for diet, obesity, alcohol intake, and exercise had a longer OS, HR 0.58 (p=0.01), and a longer DFS, HR 0.69 (p=0.03).

Gastrointestinal and Pancreatic Cancer

- Abstract 4004, S. Al-Batran et al. revealed that in patients with gastric or GE-junction cancer, neoadjuvant plus adjuvant chemotherapy with FLOT (5-FU, leucovorin, oxaliplatin, plus docetaxel) was superior to ECF/ECX (epirubicin, cisplatin, and 5-FU or capecitabine) with PFS 30 mo vs 18 mo; HR 0.75 (p=0.004), and OS 50 mo vs 35 mo (p=0.001). FLOT may be the new standard of care for resectable gastric or GE-junction cancer.
- In a practice-changing abstract, J. Primrose et al. (Abstract 4006) showed results of the BILCAP study with an OS of 53 mo with adjuvant capecitabine vs 36 mo with observation, HR 0.75 (p=0.03). This regimen is now the standard of care.
- S. Hingorani and colleagues (*Abstract 4008*) demonstrated that addition of PEGPH20 (degrades hyaluronan) to nab-paclitaxel plus gemcitabine as first-line treatment of metastatic pancreatic adenocarcinoma patients (HALO202 study) increased the PFS to 9.2 mo vs 5.2 mo, HR 0.57 (p=0.048), in patients with a high hyaluronan level.



Genitourinary Cancer Non-Prostate

- Abstract 4501, D. Bajorin et al. presented long-term follow-up of the KEYNOTE-045 trial comparing pembrolizumab with chemotherapy (paclitaxel, docetaxel, or vinflunine) in urothelial cancer patients. 18 mo OS was 36% with pembrolizumab and only 20% with chemotherapy, HR 0.7 (p=0.001).
- D. Smith and colleagues **(Abstract 4503)** showed initial results with epacadostat plus pembrolizumab with a RR of 35%. This appears to be an exciting combination.

Genitourinary Cancer Prostate

- In a plenary session presentation, K. Fizazi et al. (Abstract LBA3) studied patients with high-risk metastatic hormone-naïve prostate cancer (LATITUDE study). Patients received ADT or ADT plus abiraterone. Addition of abiraterone increased OS to 60% at 42 mo vs 34.7 mo without, HR 0.62 (p=0.001).
- In a practice-changing abstract, (*Abstract LBA5003*) N. James et al. compared the treatment of high-risk prostate cancer patients undergoing radiation, with abiraterone or without it (the STAMPEDE trial). Abiraterone improved OS by 37%, HR 0.63 (p=0.00001).
- In localized prostate cancer, A. Nabid and colleagues (*Abstract 5008*) showed that radiation therapy with either 36 mo or 18 mo of ADT gave equal OS. QOL and sexual satisfaction were better in the 18-mo group.
- In patients with recurrent prostate cancer, K. Chi and colleagues (*Abstract 5002*) showed that enzalutamide produced a 50% decrease of PSA in 73% of patients vs only 53% with abiraterone plus prednisone (p=0.004), but with similar time to PSA progression 8.0 mo vs 7.4 mo.
- Abstract 5001, M. Hussain et al. studied relapsed or recurrent prostate cancer patients with a BRCA2 mutation or other DNA repair deficiency (25% of prostate cancer patients), and showed that the addition of veliparib to abiraterone plus prednisone increased PFS to 13.8 mo vs 8.0 mo without veliparib (p=0.02).

Gynecologic Cancer

- In ovarian cancer patients at primary surgery, P. Harter et al. (Abstract 5500) showed from the LION study that omitting lymphadenectomy resulted in equivalent OS 69 mo compared to patients with complete surgery plus lymphadenectomy 65 mo. Morbidity and mortality were reduced by omitting the lymphadenectomy.
- In an important study, A. Du Bois et al. (*Abstract 5501*) demonstrated that following recurrence and chemotherapy of ovarian cancer, addition of cytoreductive surgery resulted in a longer PFS 19.6 mo compared to 14.0 mo without surgery.
- D. Matei and colleagues (Abstract 5505) showed that following endometrial carcinoma surgery with a high-risk of recurrence, adding radiation to chemotherapy did not increase PFS or OS. Completion of chemotherapy was more difficult after radiation.

Head/Neck Cancer

- In Abstract 6010, O. Hamid et al. reported a 34% RR to epacadostat (an IDO inhibitor) and pembrolizumab in third-line head and neck squamous cell cancer. Epacadostat also produced a 35% RR in urothelial tumors according to D. Smith et al. (Abstract 4503), a 50% RR in renal cell cancer in Abstract 4515 (P. Lara and colleagues), and is being studied with nivolumab in multiple tumors according to R. Perez and colleagues (Abstract 3003). This is an exciting new combination of immunotherapy.
- Abstract 101, E. Cobain and colleagues reported on 500 patients with head and neck squamous cell cancer, showing 12.2% germline mutations and tumor somatic changes in 78%, but with only 19% actually using a targeted drug. OS was 12 mo in mutation-guided therapy.
- M. Gillison and colleagues (Abstract 6019) compared nivolumab to physician-chosen chemotherapy (methotrexate, docetaxel, or cetuximab) in patients with platinum-resistant head and neck squamous cell cancer. Nivolumab produced longer OS 7.7 mo vs 3.3 mo, HR 0.56.

Health Sciences Research

 In an important plenary session paper, E. Basch and colleagues (Abstract LBA2) studied patients with metastatic solid tumors being treated with chemotherapy. Patients who were emailed a symptom evaluation form to self-report 12 symptom complexes (patient-reported outcome patients) with physician/ nurse follow-up were compared to usual care. Patient-reported outcome patients produced longer OS, 31.2 mo vs 26 mo, HR 0.83 (p=0.03), with increased QOL and 7% fewer ER visits. Physicians can implement this kind of program immediately.



- Abstract 10009, H. Singh et al. of the FDA reported on the 10-year (2005-2015) review of numbers of older adults in clinical trials. Older adults, particularly patients over 75, were under-represented in clinical trials, only 12% of patients compared to 29% of patients <75 who were diagnosed with cancer in 2013.
- Abstract 6521, X. Han and colleagues showed that after the ACA, Stage I diagnosis increased (breast cancer 48.9% after ACA vs 47.8% before, colon 23.7% vs 22.8%, and lung cancer 17.7% vs 16.6%).

Immunotherapy

- CAR-T cell therapy was one of the most exciting areas of new therapeutic approaches. Carl June, MD, of the University of Pennsylvania, received the David A. Karnofsky Memorial Award for his pioneering work on engineering T cells in targeted cancer therapy and discussed his work during the June 3 Karnofsky Lecture.
- Abstract 3008, J. Wargo et al. presented interesting data on metastatic melanoma patients being treated with anti-PD-1 immunotherapy. The gut microbiome differed in responders vs non-responders. More Clostridiales were seen in responders vs more Bacteroidales in non-responders.
- L. Derosa et al. (*Abstract* 3015) showed that in patients with renal cell carcinoma receiving anti-PD-1 therapy, receiving antibiotic from 2 mo prior up to 1 mo after therapy was associated with decreased response. PFS was 3.4 mo with antibiotic vs 5.2 mo without (p=0.01). More importantly, OS was only 12.2 mo with antibiotic vs 20.8 mo without (p=0.001).

Leukemia, Myelodysplastic Syndrome, Lymphoma

• Abstract 7500, I. Flinn et al. reported on patients with indolent non-Hodgkin's lymphoma or mantle cell lymphoma treated in the BRIGHT study. Bendamustine plus rituximab was slightly superior to standard R-CHOP or R-CVP in 5-year PFS (indolent non-Hodgkin's lymphoma HR 0.7 p=0.06 and mantle cell lymphoma HR 0.4 p=0.004).

- M. Rummel and coauthors (*Abstract 7501*) presented the StiL NHL1 study in indolent non-Hodgkin's lymphoma patients treated with bendamustine plus rituximab or CHOP-R. OS at 10 years was statistically equal (71% with bendamustine plus rituximab vs 66% for CHOP-R), but time to next treatment was better in bendamustine plus rituximab-treated patients, HR 0.52 (p<0.001). Bendamustine plus rituximab appears to be a preferable initial treatment.
- Abstract 7003, J. Altman et al. showed CR rate of 55% in FLT3 mutation-positive relapsed or refractory AML treated with gilteritinib. 20/60 patients had a deep molecular response, with OS improved to 417 days vs 199 days in patients without a deep molecular response (p<0.001).
- E. Stein and colleagues (*Abstract 7004*) reported a CR rate of 19% in relapsed AML patients with an IDH2 mutation (8-15% of AML patients) treated with enasidenib.

Lung Cancer

- In patients with small cell lung cancer, T. Owonikoko and coauthors (*Abstract 8505*) reported the results of ECOG-ACRIN 2511 study treating patients with cisplatin and etoposide with or without veliparib. PFS increased to 6.1 mo with veliparib vs 5.5 mo without veliparib, HR 0.63 (p=0.01), OS was 10.3 mo vs 8.9 mo.
- In patients with mesothelioma, A. Scherpereel and colleagues (Abstract LBA8507) showed RR 19% to nivolumab and 26% after nivolumab plus ipilimumab. OS was 10.4 mo on nivolumab, and was still 65% at 12 mo on nivolumab plus ipilimumab.
- Also in patients with mesothelioma, A. Nowak et al. (Abstract 8506) showed that treatment with pemetrexed plus cisplatin with or without nintedanib, produced OS favoring nintedanib,



HR 0.77 but p=0.3 only. PFS was better in nintedanib-treated patients, HR 0.54 (p=0.01).

- In patients with NSCLC, J. Chaft and colleagues (Abstract 8508) showed following nivolumab as neoadjuvant therapy 2 doses, 20/21 patients were resected, PR was only 10% but with major pathological response (<10% viable tumor cells) in 9/21 (43%) of patients. PD-L1 did not correlate with pathology response. RECIST response did not correlate with pathology response either.
- In patients with Stage II or IIIA NSCLC, Y. Wu et al. (*Abstract* 8500) compared gefitinib with cisplatin plus vinorelbine adjuvant therapy in patients with an EGFR mutation. DFS was superior with gefitinib 28.7 mo vs with cisplatin plus vinorelbine 18.0 mo, HR 0.6 (p=0.005).
- Abstract LBA9007, T. Mok and coauthors showed that in the ARCHER 1050 study in NSCLC patients with an EGFR mutation, dacomitinib was superior to gefitinib PFS 14.7 vs 9.2 mo, HR 0.59 (p=0.001), and OS 14.8 mo vs 8.3 mo, HR 0.4 (p=0.001).
- Abstract LBA9008, A. Shaw and colleagues showed that alectinib was superior to crizotinib in patients with ALK-positive NSCLC, with PFS not yet reached vs 11.1 mo, HR 0.47 (p<0.0001).
- T. Mok and colleagues (Abstract 9005) showed in the AURA3 trial that patients with T790M-positive NSCLC and brain metastases had good CNS responses to osimertinib; RR 70% vs only 31% with chemotherapy (p=0.015). CNS PFS was longer with osimertinib 11.7 mo vs 5.6 mo with chemotherapy, HR 0.32 (p=0.004).
- Abstract 10017, J. Malhotra et al. reported on the surveillance of over 10,000 patients with Stage I or II NSCLC. Compliance with annual imaging for recurrence or for second cancers was only 56% at 30 mo and 44% at 60 mo. OS of patients who were compliant with imaging vs non-compliant was improved, HR 0.86 at 18 mo and HR 0.68 at 60 mo of compliance.

Melanoma

- C. Robert et al. (Abstract 9504) reported long-term follow-up on KEYNOTE-006. In ipilimumab-naïve patients with metastatic melanoma randomized to either of 2 doses of pembrolizumab or ipilimumab, 33 mo OS favored pembrolizumab patients at 50% vs 39% on ipilimumab. RR was 42% on pembrolizumab vs 16% on ipilimumab. After stopping pembrolizumab at 24 mo, 23% were in CR and 23/24 continued in CR; 64/68 in PR continued in PR; and 10/12 in SD remained in SD. 91% were progression free at 12 mo after stopping.
- G. Long and colleagues (Abstract 9505) reported on long-term follow-up of dabrafenib plus trametinib. 5-year OS was 28% and even higher (51%) in patients with normal lactate dehydrogenase and <3 organs involved by melanoma.

(Abstract 9507) H. Tawbi and colleagues presented the results of melanoma patients with brain metastases treated with nivolumab 1 mg/kg plus ipilimumab 3 mg/kg, followed by nivolumab maintenance in the CheckMate 204 study. Brain CR was 21%, PR 33%, and stable 5%. Median time to response was 2.8 mo. Confirming the activity of immunotherapy, G. Long and coauthors (Abstract 9508) reported brain RR to nivolumab plus ipilimumab of 50% with a 6 mo PFS of 50%.

Multiple Myeloma

- J. Berdeja et al. (Abstract 3010) reported 6/6 responses in myeloma patients to CAR-T in study bb2121. F. Fan and coauthors (Abstract LBA3001) reported a RR of 100% with B38M CAR-T cell therapy. Additionally, in the JCAR017 trial, J. Abramson et al. (Abstract 7513) showed a 60% CR rate in relapsed NHL, and B. Shah and colleagues (Abstract 3024) reported 6/8 CR in relapsed/refractory ALL in the Zuma-3 trial.
- A. Jakubowiak and coauthors **(Abstract 8000)** described the results of a Phase Ib study of daratumumab plus KRd (carfilzomib, lenalidomide, and dexamethasone). RR was 100%, CR 43%, and 6 mo PFS was 100%.
- Abstract 8005, N. Raje et al. compared zoledronic acid with denosumab in 1,700 patients with myeloma. Denosumab was noninferior and PFS was 46 mo with renal toxicity only 10% on denosumab, but PFS was only 35 mo and renal toxicity 17% on zoledronic acid. PFS HR was 0.82 (p=0.036) favoring denosumab. There were no QOL studies done.
- Abstract 6522, A. Olszewski and colleagues showed that closure of the Medicare Part D coverage gap by the ACA resulted in reduced out-of-pocket costs for 1 year of "IMiD" therapy from \$6,502 to \$4,925 without low-income subsidies, and down to \$7 with the subsidies.



Patient and Survivor Care

- In SCORAD III, P. Hoskin et al. (*Abstract LBA10004*) showed that in patients with epidural cord compression, radiation with one fraction (one day) was equal to radiation with 5 daily fractions, resulting in ambulation at 8 weeks; 70% vs 73%.
- G. Rodin et al. (Abstract LBA10001) found that psychosocial interventions were successful in relieving distress and depression with the CALM protocol, and relieving fear as shown by J. Beith and colleagues (Abstract LBA10000).

Precision Medicine

In the ProfiLER study, O. Tredan and colleagues (Abstract LBA100) tested a 69-gene panel in 2,676 patients, with 1,944 successful profiles. 52% had an active genomic alteration, but 1/3 of those had poor performance status and were not treated. Ultimately, 7% were treated with a matched drug with an impressive OS of 3.3 years and 34.8% survival at 5 years. This is excellent data—showing value in selected patient groups.

Sarcoma

Abstract LBA2501, D. Hyman and colleagues showed an RR of 76% in patients with tropomyosin receptor kinase-mutated soft tissue sarcomas treated with larotrectinib, resulting in 75% of all patients being able to undergo surgical resection. 12% of patients had a CR.

Tumor Biology

- Abstract LBA100, O. Tredan and coauthors presented the results of molecular analysis with targeted exon sequencing and comparative genomic hybridization of 2,590 patients in the ProfiLER study. 51.5% had at least 1 actionable mutation. A molecular tumor board recommended mutation targeted therapy in 644 patients and 101 started the recommended therapy. PFS was 2.8 mo in those patients, RR was 2.3% CR, and 15.1% PR. At 6 mo 24% are alive and progression free.
- N. Ammakkanavar et al. (*Abstract 102*) showed a 9% change in therapy with next generation sequencing in 250 patients, with a PFS of 5 mo and an average cost of \$10,000.

Closing Thoughts

ASCO 2017 was an interesting meeting, giving attendees valuable information that will help them manage their practices and change the way they treat their patients. Be sure to review the abstracts on the ASCO website and the subsequently published manuscripts to be confident of the results, side effects, and clinical interpretations.

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